INSTITUTO POLITÉCNICO DE LISBOA

ESCOLA SUPERIOR DE TECNOLOGIA DA SAÚDE DE LISBOA

STEREOTACTIC BODY RADIATION THERAPY IN LUNG CANCER PATIENT POSITIONING: ARMS UP *vs.* ARMS DOWN A DOSIMETRIC EVALUATION

CÁTIA BARREIRA

Orientadora: PROF. MARGARIDA EIRAS

MESTRADO EM RADIAÇÕES APLICADAS ÀS TECNOLOGIAS DA SAÚDE – Terapia com Radiações

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“Your work is going to fill a large part of your life, and the only way to be truly satisfied is to do what you believe is great work. And the only way to do great work is to love what you do. If you haven't found it yet, keep looking. Don't settle. As with all matters of the heart, you'll know when you find it.”

Steven Paul Jobs

RESUMO

A radioterapia estereotáxica (SBRT) tem mostrado bons resultados no tratamento do cancro do pulmão. O movimento respiratório dos órgãos depende do doente, da posição dos braços e da imobilização. Esta pode ser feita com ou sem a ajuda de acessórios como o compressor abdominal que quando os tumores são localizados nos lobos inferiores e perto do diafragma se torna vantajoso, mas se for colocado com elevada pressão pode aumentar o movimento respiratório. O posicionamento sem acessórios rigidos de imobilização deve ser acompanhado de imagens diárias para minimizar os erros de *set-up* e ter uma elevada precisão no volume a irradiar. O objectivo deste estudo é fazer uma avaliação dosimétrica de planeamentos de SBRT com arcoterapia volumétrica de intensidade modulada (VMAT) em dois posicionamentos diferentes: braços para cima e braços ao longo do corpo. Numa amostra de quatro doentes, para cada posicionamento foram adquiridas imagens de Tomografia Computorizada (TC) e imagens de quarto Dimensões de Tomografia Computorizada (4DCT) e tendo sido foi feita uma reconstrução *mid-ventilation*. Foram estudadas várias variáveis, entre as quais, volumes e doses para os volumes-alvo e órgãos de risco e unidades monitor. Não foram encontradas diferenças significativas entre as variáveis estudadas. Podendo concluir-se que o posicionamento do doente deve ser escolhido de acordo com as suas dificuldades, devendo ser confortável, estável e reprodutível. Em alguns casos, e em doentes em que o movimento respiratório seja de grande amplitude, o posicionamento com os braços ao longo do corpo pode ter a vantagem de diminuir o movimento respiratório e consequentemente o volume alvo interno (ITV).

Palavras-chave: radioterapia esterotáxica (SBRT); cancro do pulmão; imobilização do alvo; posicionamento; posição dos braços.

ABSTRACT

Stereotactic Body Radiation Therapy (SBRT) has been shown good results in lung cancer patients. Respiratory motion of internal organs depends on patient, arms position and the type of immobilization devices used. For patient immobilization can be used rigid fixation devices or not. Abdominal compression can be advantageous for lung tumors in lower lobe or close to diaphragm, but if placed with too much pressure it can increase tumor motion and target volume. Without rigid fixation devices daily images are important to minimize set up errors and have high precision in the irradiated volume. The aim of this study is to evaluate dosimetric SBRT plans with Volumetric Modulated Arc Therapy (VMAT) in different positions: arms up and arms down. Four SBRT lung cancer patients were included in the sample. A Computed Tomography (CT) and a four-Dimensional Computed Tomography (4DCT) was acquired and a mid-ventilation was reconstructed. The analyzed variables were volumes, doses – targets and oragans at risk – and total of monitor units (the sum of all arcs). No statistically significant differences were found between the studied variables. Patient position should be chosen according to patients' difficulties and comfort in order to make a comfortable, stable and reproducible position. In patients with a large respiratory motion amplitude, position with arms down can have advantages because respiratory motion decreases, decreasing the margins for internal target volume (ITV).

Key-words: SBRT; lung cancer; target immobilization; patient position; arms position; arms up; arms down.

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Introdução geral

O cancro do pulmão é um dos cancros com maior taxa de mortalidade, a nível mundial. Para esta patologia, existem várias terapêuticas, sendo a cirurgia a terapêutica mais recomendada. Muitas vezes existem co-morbilidades por parte do doente, ou até localizações anatómicas que a tornam impossivel de executar. Nestes casos, são analisadas outras opções terapêuticas como a quimioterapia e/ou radioterapia. A radioterapia é um tratamento alternativo para tumores inoperáveis e para metátases. A radioterapia estereotáxica (SBRT) é uma técnica que utiliza o escalonamento de dose para um maior controlo tumoral. Esta, tem como principal característica a dose biológica efectiva (BED), pois é administrada ao doente uma elevada dose num curto período de tempo, 1 a 5 frações, enquanto minimiza a dose nos tecidos adjacentes, sendo feita através de uma alta precisão no alvo, doses conformacionais e consequentemente um elevado fall-off de dose. Deste modo, o posicionamento e a sua reprodutibilidade assumem uma elevada importância, podendo ser execuíveis através de dispositivos de imobilização rigidos ou não-rigidos. Apesar disto, a posição dos braços continua um tema por estudar. O posicionamento e o conforto do doente tornam-se aspetos muito importantes na utilização de técnicas que administram uma elevada dose. O doente deve estar posicionado confortavelmente com a ajuda dos acessórios de posicionamento onde o seu peso deve ser distribuído uniformemente durante. O posicionamento standard utilizado para tumores do pulmão é a colocação dos braços para cima, contudo, este nem sempre é possivel devido às co-morbilidades dos doentes. Neste seguimento, o posicionamento é feito com os braços para baixo, surgindo a necessidade de estudar o tema, através de uma comparação dosimétrica, feita em doentes com tumores de pulmão. Para isso foram comparados planeamentos com a técnica arcoterapia volumétrica de intensidade modulada (VMAT) aplicando uma fracção única de 24Gy.

O objetivo deste projecto de investigação é fazer uma revisão de literatura que enquadre a importância do posicionamento em tumores do pulmão, assim como, perceber se o posicionamento com os braços para baixo pode ser uma opção de posicionamento sem prejuizo para a qualidade/caracteristicas dosimétricas do planeamento.

Os artigos que se seguem foram construídos em inglês com vista a serem publicados em revistas internacionais da área e por este motivo, são os únicos elementos em língua estrangeira.

Stereotactic Body Radiation Therapy in lung cancer: patient positioning and target immobilization – a literature review

Cátia Barreira[1]; Margarida Eiras, PhD[2];

[1]Student of master: Radiations Applied to Health Technologies – Radiation Therapy
Corresponding author: catiabarreira@hotmail.com
[2]Escola Superior de Tecnologias da Saúde de Lisboa

Abstract: Lung cancer is the leading cause of cancer-related deaths worldwide. Radiotherapy is an alternative treatment for inoperable tumors and also for patients with slow growing metastatic lung tumors. Dose escalation has been an important issue to improve local tumor control and overall survival. Stereotactic Body Radiation Therapy has been gaining a large interest over the past few years, using high dose per fraction, sharp dose gradients and high-precision target localization. Respiratory motion of internal organs depends on patients, arms patient position and the type of immobilization devices used. Patient immobilization can be enforced with or without rigid fixation devices. Abdominal compression can be advantageous for lung tumors in lower lobe or close to diaphragm, but if placed with too much pressure it can increase tumor motion and target volume. Despite of this we can conclude that all positions have advantages. Without rigid fixation devices daily images are important to minimize set up errors to have high precision in the irradiated volume. With technology available in the treatment room and with advanced treatment planning systems, a question for the future can be made "Are arms above head, in lung cancer patients, the only option to achieve a good dosimetric plan?"

Keywords: SBRT; lung cancer; patient immobilization; respiratory motion; arm position.

1. Introduction

Lung cancer is the leading cause of cancer-related deaths worldwide.[1] Surgery remains the treatment of choice but many patients are inoperable due to their compromised pulmonary reserve, cardiac function, or significant co-morbidities.[2-5] Radiotherapy is an alternative treatment for inoperable tumors and also for patients with slow growing metastatic lung tumors.[6] Traditionally this treatment has a total dose of 50-70 Gy in 1.8-2 Gy per fraction.[2,4,6] Dose escalation has been important to improve local tumor control and overall survival.[4,6] However, dose escalation by conventional fractionated radiotherapy has the risk of increasing normal tissue toxicity.[6] Stereotactic Body Radiation Therapy (SBRT) has been gaining a large interest over the past few years, in small target volumes because uses high doses in 1-5 fractions and increases the local control.[2,7,8] This technique also uses sharp dose gradients and high-precision target localization (image in the treatment room).[2,5,8,9] To reduce uncertainties in targeting, important technical considerations in SBRT include:[10]

1) stable and reproducible patient positioning;
2) high-quality imaging for treatment planning;
3) accurate target and Organs At Risk delineation (OAR);
4) advanced treatment planning algorithms;
5) image-guidance systems capable of performing in the sub-millimeter range;
6) robust quality assurance methods.

Excessive intra-fraction patients' motion compromise target and OAR dose distribution.[10] Two important factors are patients' position and immobilization. This literature review has the aim to enlighten the major issues in patient position/target immobilization in lung cancer patients.

2. Materials and methods

For this review, the main databases specialized in systematic reviews were used: B-ON, PubMed, SciELO, Cochrane Library, Research Gate and RCIPL (Scientific Repository produced by Instituto Politécnico de Lisboa). The first search was made with the key words – SBRT; lung cancer; patient immobilization; patient position - and sixty-six articles were found. After reading all the abstracts eighteen articles were selected. From these articles the references were analyzed and twelve more articles were added. In total thirty articles were included in this literature review, five of them were already literature reviews and were included because it add value to this review. There was no filter applied in terms of time line because SBRT is a relatively recent technique, neither in terms of patient follow-up. For that, inclusion criteria were:

1) Treatment type: SBRT;
2) Patient type: only patients with primary or metastatic lung cancer;
3) Results measurements: dosimetric data from comparison of distinct positions, tumor tracking and immobilization; respiratory motion.

Scientific literature published between January 1999 and June 2015, was systematically reviewed. Table1 shows summary of the most important criteria found in the analyzed articles.

3. Results

3.1 Intrafractional tumor motion

At rest, a healthy person breathes 12 to 15 times per minute. Respiratory motion, volume and frequency – in the same person – can change with biochemical conditions, body position, abdominal contents and emotional conditions.[11,12] Respiratory muscles motion is also altered by pathological conditions as pleural adhesion after pleuritis, thoracic surgery, thoracic irradiation, diabetes mellitus, hypothyroidism, chest pain, malnutrition and muscle fatigue. Respiratory motion of internal organs depends on body´s position, arms' position and the type of immobilization devices used.

Inspiration requires contraction of diaphragm and external intercostal muscles located between the ribs. Diaphragm contraction causes it to move downward and increases vertical dimension of thoracic cavity. Diaphragm contraction produces a 75% change in intra-thoracic volume during resting inspiration. External intercostals contract to elevate lower ribs and push the sternum outward, increasing the anteroposterior dimension of thoracic cavity. Lung volume is different between inspiration and expiration at the same pressure. In voluntary active expiration, internal intercostal muscles contract and pull the rib cage downward, and abdominal muscles increase abdominal pressure which forces the diaphragm up.[11] Many authors studied the mean amplitude in superior-inferior (SI) direction and found that tumors in lower lobes and not attached to rigid structures had a larger motion than tumors in upper-lobe.[11-13] Plathow et al. studied safety margins of 3.4mm for tumors in upper region, 4.5mm for middle region and 7.2mm for lower region.[13] Shirato et al. showed that cardiac motion influence in tumor motion between 1 to 4 mm in left-right (LR) axis and 1 to 2 mm in remaining axis.[11] Factors as comorbidities, performance status, age and gender can influence intrafractional target shifts. It is known that patients older than seventy-five had larger shifts during treatment and the male patients had larger shifts than females.[5, 14,15]

3.2 Patient positioning

The most important SBRT characteristic is delivery of higher biologic effective dose (BED) over a shorter period of time, while minimizing normal tissue exposure to high dose radiation.[9,16,17] That is only possible with two major characteristics: patient position and image guided systems in the treatment room. Position should offer comfort to patients, reproducibility and accuracy to treatment. Patient immobilization can be enforced with commercially available devices – rigid fixation devices - e.g. stereotactic frames, vacuum systems or thermoplastic masks to reduce set-up uncertainties[12,18] or without rigid devices to immobilize the patient but with motion-controlled treatment systems.[2,5,14,17]

3.2.1 Rigid fixation devices

Several articles reported patient position with stereotactic frame. One of the most important steps in patient positioning for SBRT is ensuring that patients are comfortably immobilized in the frame, the weight has to be uniformly distributed and supported to avoid patient's tendency to readjust his weight during treatment.[19] Authors concluded that a frame-based position allows a simple and effective tumor motion control[8,18,19] and a better target position accuracy.[4,16]Waldeland et al. analyzed thirty patients positioned with stereotactic frame and abdominal compression, showed that conventional margins applied to the tumor were sufficient to cover the Internal Target Volume (ITV) by the prescription dose.[20] Gutierrez et al. showed with twenty lung cancer patients that both BodyFix® and Body Pro-Lok^{TM} systems were user-friendly, fast to position and immobilize the patient providing reproducible, accurate and efficient positioning.[8,21] Shah et al. concluded that stereotactic frame is more accurate than other position devices, saying that with stereotactic frame a 5 mm target margin appear adequate to incorporate ITV but do not appear to be sufficient for BodyFix® immobilization.[4]

Abdominal compression

Abdominal compression plate is placed on patient's abdomen 3 to 4 cm below the costal margin of the ribs and below the xiphoid. The placement of this compressor is critical, if it is placed in a superior position it can be a potential to fracture ribs if enough pressure is applied and if it is placed too low it is less effective in decreasing diaphragm motion.[19] Several authors reported the advantage of using the abdominal compression,[9,16,22] reforcing it as a major advantage in tumors in the lower lobes[2,12,16,23] and in lesions close to the diaphragm. If tumors are large enough, abdominal compression can be associated with an interesting ITV reduction. For other lobes, the compressor can provide a smaller benefit or even induce unwanted effects such as larger tumor motion and ITV increase.[3,12,24,25] That is why most of the authors reported that abdominal compressor should be used only when it adds advantages to tumor motion control.[12,23] Negoro et al. showed with eighteen patients, that the tumor motion decreases from 8-20mm to 2-11mm with abdominal compression and stereotactic frame. They concluded that this immobilization had the disadvantage not to detect patients rotation along the body axis.[22] Han *et al.* found that abdominal compression is superior reducing SI and overall respiratory tumor motion and it is faster in set-up time and more comfortable, than *BodyFix*®. Intrafraction tumor motion had no significant difference between three positions.[2]

Thermoplastic masks

Despite of being a usual positioning device in head and neck cancer, in thoracic cancer it is not very common to use thermoplastic masks. Aoki et al. analyzed twenty patients ($T_{1-2}N_0M_0$ and tumor respiratory movement no more than 10mm) position with both arms raised and immobilized with a mask with a custom-made head rest. These authors concluded that, for SBRT with a 54 Gy total dose in nine fractions, this position can be an alternative for lung cancer patients because they can achieve an acceptable tumor motion control.[26] Other authors compared vacuum cushions and thermoplastic masks in 73 fraction, 246 CBCT images analyzed and their results showed that thermoplastic mask can offer a better and easier reproducibility and significantly less intrafraction set up displacements, when compared with vacuum cushions.[16]

3.2.2 Non rigid fixation devices

With the technology used in the treatment room, some authors argue that positioning can be changed and made it simple for the patient.[2,5,14,17] Authors observed that a rigid tight whole body immobilization can cause a certain patient discomfort during treatment and that can cause patient movement.[14,15] Several articles analyzed showed that the image before, during and or after treatment can improve the shift results using a simple position without stereotactic frame.[2,5,6,27] Alderliesten et al. concluded with thirty-six patients that the accuracy found for 3D surface imaging system is sufficient for monitoring intrafraction tumor motion purposes in frameless SBRT for female patients.[5] Dahele et al. studied thirty patients with their arms above head and a foam to support their knees, with Real-time Position Management (RPM) and treatment planning with Volumetric Modulated Arc Therapy (VMAT). In this study they concluded that it is possible to make a stable position without rigid immobilization for SBRT patients.[10] Sonke et al. treated sixty-six tumors without a rigid immobilization and with free breathing, reported that this positioning can be precise when treatment is guided with 4D-CBCT. These authors concluded that the use of alpha cradle and the body frame increase skin dose and are logistically more challenging than a non-rigid positioning.[17]Shen et al. showed a major role of Active Breathing Control (ABC) even with frame positioning. Respiratory tumor motion was less than 3mm, but without ABC technique helping to control tumor motion they recommend a uniform PTV margin of 5mm axial and 10mm SI to be added for stereotactic lung radiotherapy when image guidance is not used.[6] This conclusion it is supported also by other authors.[28,29]

4. Discussion

To irradiate the tumor precisely and to decrease irradiated volume of OAR, various methods have been developed. The American Association of Physicists in Medicine classified five major categories: [30]

1) Motion-encompassing method;
2) Respiratory-gating method;
3) Breath-hold method;
4) Forced shallow-breathing with abdominal compression method;
5) Real-time tumor-tracking method.

This shows the importance of considering both patient, target tumor and motion-management strategy for high-precision radiotherapy.[10] In various articles the conclusions about respiratory tumor motion are very enlightening. Tumors in lower lobes had the largest variations and in these tumors abdominal compression has advantages decreasing tumor respiratory motion, if it is well placed, because of that, abdominal compression should be evaluated during the CT scan, otherwise it can increase respiratory tumor motion.

Patient position should have a balance between patient comfort, accuracy and reproducible position for treatment, if these parameters aren't accomplished we can compromise the treatment and increase set up errors. Before, SBRT was done only with stereotactic frame, after many position studies rigid position can be replaced to a simple positioning. Balance between patients' position and use of rigid devices need to take into account the type of image technology available in the treatment room. For example, a non-rigid positioning is acceptable when image acquisition is daily.

5. Conclusion

Despite of this we can conclude that all positions have advantages but it is important in SBRT minimize set up errors and have high precision in the irradiated volume.

In lung cancer patients, one of the most important issue is patient performance status, and the positioning should be adapted according patient limitations. With that and technology available in the treatment room, a question for the future can be made "Are arms above head, in lung cancer patients, the only option to achieve a good dosimetric plan?"

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Table 1 - Summary of the most important criteria in the analyzed studies

Criteria	Number of studies
Sample size:	
- n < 30	11
- n ≥ 30	14
- Reviews	5
Type of study:	
- Comparative	8
- Descriptive	22
Main theme:	
- Patient positioning	12
- Target immobilization	9
- Patient positioning and Target immobilization	9
Total:	**30**

Stereotactic Body Radiation Therapy in lung cancer: arms up *vs.* arms down - a dosimetric evaluation

Cátia Barreira,[1] Margarida Eiras,[2] Sandra Vieira,[3] Paula Buitrago,[3] Graça Coelho,[3]
Nuno Pimentel,[3] Carlo Greco[3]

[1]Student of master: Radiations Applied to Health Technologies – Radiation Therapy
Corresponding author: catiabarreira@hotmail.com
[2]Lisbon School of Health Technology
[3]Radiation Oncology Department, Champalimaud Foundation for the Unknown - Lisbon

ABSTRACT

Aim: The aim of this study is to evaluate dosimetric Stereotactic Body Radiation Therapy (SBRT) plans with Volumetric Modulated Arc Therapy (VMAT) in lung cancer with different positions: arms up and arms down.

Materials and methods: Four SBRT lung cancer patients (2 males and 2 females) were included in the sample. A Computed Tomography (CT) and a four-Dimensional Computed Tomography (4DCT) was acquired and a mid-ventilation was reconstructed for each position. The analyzed structures were: volumes – CTV, ITV, PTV and organs at risk (OARs), maximum dose (Dmax), mean dose (Dmean) and minimum dose (Dmin); OARs - Dmax, Dmean and the dose received by the volume (cc) specified by the constraints; V_{10Gy}, V_{15Gy} and V_{20Gy} – as the volume receiving (x) Gy for the lung; Total of monitor units (the sum of all arcs); Volume that received 6, 12, 18 and 20.4 Gy.

Results: No statistically significant differences were found, but the following values were lower with arms up: target volumes, heart volume; lung total - Dmean; spinal cord - the dose received by 1.2 cc; the volume that received 6, 18 and 20.4 Gy and the spherical diameter of the volume that received 18 Gy. The lung volumes –right, left and total- were lower with arms down.

Findings: There were no statistical differences between plans, despite of the position with arms down having more tissue irradiated, that doesn't compromise PTV coverage and it doesn't mean more dose in OAR. Patient position should be chosen according to patients' difficulties and comfort in order to make a stable and reproducible position.

Keywords: SBRT; lung cancer; patient positioning; arms up; arms down; dosimetric evaluation

1. Introduction

Stereotactic Body Radiation Therapy (SBRT) is an effective alternative for inoperable early stage lung cancer and lung metastases.[1-4] SBRT delivery high doses in 1-5 fractions to improve local tumor control.[1,5] The most important SBRT characteristic is higher biologic effective dose (BED) over a short period of time, while minimizing the normal tissue exposure.[4,6-11] This technique can only be done with high target precision, reduced tumor margins, high conform prescription dose, sharp dose fall-off away from the target, as well as mechanical requirements such as rigid immobilization and accurate patient positioning.[3,4] Typically a four-Dimensional Computed Tomography (4DCT) is used o estimate target motion.[5] The 4DCT is a correlation between Computed Tomography (CT) image acquisition with breathing cycle, to analyze the variables that affect respiratory motion which allows to contour the target margins.[4,5,12] Minimizing normal tissue irradiation in SBRT by using 4DCT scans can reduce the risk of late normal tissue toxicity associated with hypofractionated SBRT schemes.[12] The success of SBRT is based on accurate treatment planning and accurate treatment delivery. In lung cancer different uncertainties have been described, which can reduce the treatment accuracy.[4,13] Patient immobilization can be achievable with rigid devices like stereotactic frame or vacuum systems[1,3,14,15] or can be achievable with non-rigid devices.[7,16-18] Arm position remains an unexplored area of research. While most lung cancer patients are treated with their arms up, many are frail and unable to comfortably maintain this position. It has been assumed that plans with beams entering through the arms are suboptimal and also particularly sensitive to arm repositioning variability.[19] With Volumetric Modulated Arc Therapy (VMAT) it is possible to avoid the angle irradiation where arms could be included in the beam. It is possible that treating with arms down might improve patient stability and comfort, which decreases movement during setup and treatment, leading to improved dosimetric accuracy, and that adverse dosimetry of beams entering through the arms would be ameliorated by an arc geometry.[19]

The aim of this study is to understand if it is possible to have a SBRT-VMAT dosimetric plan with arms down that achieve the same dosimetric goals as the plan with arms up.

2. Materials and Methods

2.1Patient eligibility

Since February to May 2016 all lung cancer patients with medical indication for SBRT were followed. Patients were excluded for the sample:

1) Patients with nasogastric tubes;
2) Patients that planning images were acquired only in the PET-CT (Positron Emission Tomography-Computed Tomography) – software reconstruction problems;
3) Patients without the 4DCT well reconstructed.

All four patients in the sample (2 males and 2 females) went through a process where many steps were taken (fig.1).

2.2 Patient immobilization and CT acquisition

The first step in patient position for SBRT is ensuring that patients are comfortably immobilized in the position that they will be treated. A comfortable immobilization is when patient's weight is uniformly distributed and supported.[20] All four patients were positioned with an arm support which provides comfort to patients' upper body. This device has a headrest and an arms support that can be changed in order to adapt to patients' anatomy. An abdominal compression was applied by an inflatable abdominal compressor that was placed approximately 3 to 4 cm below the costal margin of the ribs and inferior to the xiphoid. This compressor was inflated to have a comfortable pressure, balancing the fact that too much pressure will increase respiratory motion amplitude. For that, pressure was adapted for each patient. Patients were instructed to have a free breathing during image acquisition, and to avoid deep respiratory or breath-hold movements. All the CT were acquired with *Philips Brilliance Big Bore (software version 2.4.10*). Respiratory cycle signal was monitored with *Bellows System (Philips Medical Systems)* a non-metallic system to avoid image artifact. This system uses an elastic strap that was attached above the abdominal compressor at the xiphoid to record the respiratory signal. Thoracic movement with respiration was detected by a sensor and this generates a waveform signal that represents the respiratory cycle. The software has graphical information about patients' respiratory cycle and acquires images in 10 respiratory cycles - 10 phases. Reconstruction is automatically made by Philips software. The phases were defined as 0% to 100%, that means each phase represents 10% of acquired respiratory motion and each phase has the same number of slices, nearly 150 slices. For all patients, the first step was CT acquisition with arms up after that 4DCT was acquired. After this procedure position was change and it was acquired the CT and 4DCT with arms along the body (arms down). In arms down no precautions were taken in terms of reproducibility. After image acquisition, 4DCT images and CT images were analyzed to make sure that they were well reconstructed.

2.3 Mid-ventilation reconstruction process

The major intra-fractional geometrical uncertainties in lung cancer treatment are due to respiratory and cardiac motion.[21,22] By eliminating these uncertainties, it allows a margin reduction, and it decreases volume of irradiated normal tissue which allows a dose escalation. A single free-breathing CT is often used for radiotherapy planning for lung tumors. However, respiration-induced tumor motion during acquisition causes artifacts in tumor shape and position, because CT acquires a stack of images without time information from the tumor motion, thus obtaining a set of arbitrary snapshots of moving structures. To overcome this problem, time-resolved 4DCT scanning techniques were developed. This set provides temporal and spatial motion information that can be used to optimize treatment-planning. However, the available commercial treatment-planning systems cannot handle a 4D CT data set as input for treatment-planning.[23] To be able to make a reliable comparison between both CT images (arms up vs. arms down) a mid-ventilation reconstruction was performed to reform the images as they were in the same respiratory cycle position. For each patient the mid-ventilation process was repeated twice, for arms up and for arms down. For both processes the same reference phase was chosen, the steps are represented in fig.2.

2.4 Contouring organs at risk and target volumes

Each patient had two mid-ventilation CT, for both mid-ventilations the same Organs At Risk (OAR) and target volumes were contoured, except for patient2 it was the only patient with humerus contoured, as it is shown in table 1. For target volumes: Clinical Target Volume (CTV), Internal Target Volume (ITV) and Planning Target Volume (PTV) were contoured. All volumes were contoured by the same person to avoid intra and inter-observational errors and contouring variations, corrected by the same Radiation Oncologist. CTV was contoured with both anatomical and biological information (PET). From CTV to ITV one margin of 2 mm isotropically was added, to account for residual errors in patient position. But, as we know tumor respiratory motion is likely to be anisotropic,[24] after analyzing and measuring respiratory motion in 4DCT, margins were changed in the directions where movement was larger than 2 mm. PTV was created from ITV adding a symmetric margin of 3 mm. A ring-shaped volume was created in all patients to achieve a conformational dose around PTV, it was created automatically from PTV with a 20 mm and 5 mm outer margin from PTV (fig.3a). For patient1 a volume (PTVcalc) was created through the sum of three PTVs (fig.3b). For patient 3 and 4, PTV included OARs and, for them a PTVcal was created, an automatic subtraction of OAR from PTVs.

2.5 VMAT plans

Rapidarc®(Varian) is a relatively recently introduced VMAT technique based on simultaneous optimization of Multi-Leaf Collimator (MLC) shapes, dose rate and gantry rotation speed. In this article, VMAT is defined as a technique with the characteristics above-mentioned.

The first step was to create a plan and specify if plan intention: curative. After this, the number of fractions and total dose needed to be defined, as well as the machine to treat this plan – *TrueBeam*® (Varian). Dose prescription was 24 Gy in one fraction, for all patients. The energy defined was 10 MV - FFF (Flattening Filter Free) with dose rate of 2400 MU/min. In this study, all the dosimetric plans were made with VMAT, arc therapy with continuous radiation delivery is a potentially decreasing treatment time per fraction without compromising the target coverage. One VMAT advantage is to have a IMRT quality plans delivered in less time, which means a decrease in intrafraction variation. Despite of this, VMAT plans have a major disadvantage – lower doses over a large volume, increasing the probability of second malignancies.[25,26] In the plans, energy 10 MV-FFF was used because it has the advantage of a higher maximum dose rate of 2400MU/min possible on Varian linear accelerators, compared with 1400MU/mim for 6MV-FFF.[26] The isocenter was chosen in PTV geometrical center of each CT. After that, arc geometry was defined, as well as the number of arcs - two or four arcs were used. All arcs, collimator and MLC were constructed to fit PTV or PTVcalc. The plan was calculated with the algorithm AAA - Anisotropic Analytical Algorithm (*version 11.0.31*) and were optimize to have the following dosimetric goals:

1) To have a good dose coverage - minimum 98% in PTV or PTVcalc;
2) To have hotpoints - maximum under 111% - inside CTV;
3) To have a 50% and 75% isodoseline uniform around PTV;
4) To have all OAR with an acceptable dose according table 2 dose constraints for SBRT-single dose of 24Gy.[27]

In some plans these characteristics could not be followed, but all the plans were approved by the same physical engineer.

2.6 Evaluation criteria and statistical analysis

The following structures were analyzed:

1) Volumes: targets and oars;
2) Target: CTV, ITV and PTV – maximum dose (Dmax), mean dose (Dmean) and minimum dose (Dmin);
3) OARs: Dmax, Dmean and the dose received by the volume (cc) specified in table 2 (eg: the dose received by the trachea in 4cc);
4) V_{10Gy}, V_{15Gy} and V_{20Gy} – as the volume receiving (x) Gy for the lung;
5) Total of monitor units (the sum of all arcs);
6) Volume that received 6, 12, 18 and 20.4 Gy that represents 25, 50, 75 and 85% of prescribed dose;
7) The spherical diameter of the volume above-mentioned.

It was performed by Wilcoxon Test in the statistical program SPSS *(version 22.0)*. The p-value less than 0.05 was considered statistically significant.

3. Results

3.1 Patients tumors and anatomic characteristics

-***Patient 1*****:** no anatomic differences were found between contoured volumes.

-***Patient 2*****:** CTV was in lung upper lobe. The comparison between contoured volumes in both CT scans shows differences: when patients have arms down CTV becomes closer to thoracic wall and brachial plexus is lower. Because of that, there are dose differences in these OAR. Because CTV was in superior lobe, humerus was contoured. When patient has arms down the humerus is lower and receives more dose: Dmax 2.4 *vs.* 6.3 Gy and Dmean 0.2 *vs.* 1.5 Gy (arms up *vs.* arms down).

-***Patient 3*****:** no anatomic differences were found between contoured volumes.

- ***Patient 4:*** There were no differences between CTV anatomic localization, in both positions and because CTV was in middle lobe. There are differences in amplitude of respiratory motion, as fig.4 shows with the graphic scale. With arms up the scale amplitude is [-6 ; 6] mm and with arms down the scale amplitude is [-0.15 ; 0.30] mm. That difference in the respiratory amplitude can be justified with the fact that the patient was overweight and with arms down it was easier to breathe. For the plan with arms down, an avoidance sector was made like it should be done if the plan was irradiated.

3.2 Statistical results

Comparing the plans, there is no statistically significant differences between all the variables, despite of that, we can conclude:

1) Volumes:
    i. all the target volumes are slightly smaller with arms up (PTV and CTV p-value=0.068 and ITV p-value=0.066);
    ii. The lungs (right, left and total volume) are slightly smaller with arms down (p-value=0.068)
    iii. The heart is slightly bigger with arms down (p-value=0.068)
2) Targets:
    i. PTV - Dmin with arms down is slightly lower (fig. 5).
3) OARs:
    i. Lung total volume (the sum of right and left lung) - Dmean had a lower value with arms up (p-value=0.066 and mean=2.9 *vs* 3.1 Gy);
    ii. Spinal cord - the dose received by 1.2cc had a lower value with arms up (p-value=0.068 and mean=4.2 *vs* 5.43 Gy).
4) V_{10Gy}, V_{15Gy} and V_{20Gy} - these values are slightly larger when patients are with arms down (table 3).
5) Total of monitor units: in three patients the sum of monitor units is larger with the arms up (table 4), but the variability of data and the range larger with the arms up

[8000;13701] make the data with no statistically significant difference (p-value= 0.144 - fig.6).

6) Volume that received 6, 18 and 20.4 Gy had a lower value with arms up (p-value=0.068 and mean: 1380.86; 303.4; 6.08; *vs* 1550.97; 329.93; 263.76 cc respectively).
7) The spherical diameter of the volume that received 18 Gy had a lower value with arms up (p-value=0.066 and mean=6.55 *vs* 6.95 cm).

4. Discussion

The aim of this study is to evaluate dosimetric plans with different arm position and make a comparison between them, to see if it is possible to achieve the same dosimetric goals for both plans. Our results show that, from a statistical standpoint, there were no differences between plans. Despite arms down having more tissue irradiated, this position doesn't compromise PTV coverage and it doesn't mean more dose in OAR.

The type of immobilization devices selected can decrease dose to the target volume and decrease tumor control rate.[28] Solberg *et al.* were treating patients with their arms at their sides, with a full-length vacuum bag, to provide a better reproducibility and to improve patient comfort.[29] Shultz *et al*. studied in fourteen patients the dosimetric evaluation between two different plans. All of his fourteen patients were treated with arms down, and to be able to make a comparison between both positions, they remove the arms digitally. In their conclusions they found statistically significant differences between PTVmax and conformity index defined as the ratio of the 50% isodose volume to PTV volume, however, the absolute differences were both less than 5%. They also showed differences in the percent of total lung tissue receiving a minimum dose of 10, 20 or 30Gy: V_{10Gy}, V_{20Gy} and V_{30Gy}. They concluded that there is no evidence to support the hypothesis that with arms down lead to clinically loss of plan quality in thoracic SBRT when VMAT is used.[19]

Patients with thoracic and abdominal cancer are commonly positioned with arms up, despite the arm position not being specified by the Radiation Therapy Oncology Group (RTOG). Position with arms up is the first choice because of three concerns: [19]

1) Beam attenuation by ipsilateral arm which can be translated as an inferior dosimetry;
2) Arm location is difficult to replicate from the setup to treatment which can affect the dosimetry accuracy;
3) The treatment with arms down imposes unnecessary radiation exposure to the arm which can be translated, later in secondary malignancies.

In SBRT one of the major concerns is secondary effects of a high dose in lung tissue. Another concern of toxicity were the effects on the central bronchus, pulmonary artery, esophagus, heart and spinal cord, for which a hypofractionated dose had not been followed up for a sufficiently long time.[30] The biggest advantage in SBRT is the higher BED. The various doses and dose fractionation combination used in lung cancer are easily compared by the use of BED. Several articles concluded that higher BED (≥100Gy) achieves high rates of local control.[31-33] But to do this technique a good technology in the treatment room is necessary.

In this study no statistically significant differences were found, so we can conclude that patient position should be chosen according to patients' co-morbidities and comfort in order to make a stable and reproducible position. In patients with a large respiratory motion amplitude, position with arms down can have advantages, decreasing respiratory motionand margins for ITV and with that the PTV. Despite of not finding statistically significant differences between the monitor units, we believe that the position with the arms up had larger values because, in all patients, it was the first plan that was made, and only after finding the ideal plan, we were able to plan the patients with the arms down. In comparison between the volume that received 6,18 and 20.4 Gy, it is understandable that, with the arms up the values were lower. For that, we can conclude that arms position need to be balanced between patients' amplitude respiratory motion, co-morbidities and the fact that with arms down it will irradiate more volume of healthy tissue despite of lung volume can be smaller.

This study had limitations: the biggest limitation was sample size with only four patients we cannot generalize the results for all the population. Another limitation was the fact that arm reproducibility was not taken into account in positioning with arms down. We know in fact that arms' position and their rotation can affect treatment accuracy. Despite of this, planning with VMAT, is clinically possible to do an avoidance sector from one rotation angle to another one which included the arms.

5. Conclusion

We find no evidence to support the hypothesis that arms down position leads to a clinically significant loss of plan quality, when SBRT-VMAT is used for a single fraction of 24 Gy in lung cancer patients. For that, and for more conclusions we suggest more studies to be able to have a generalized conclusion.

6. References

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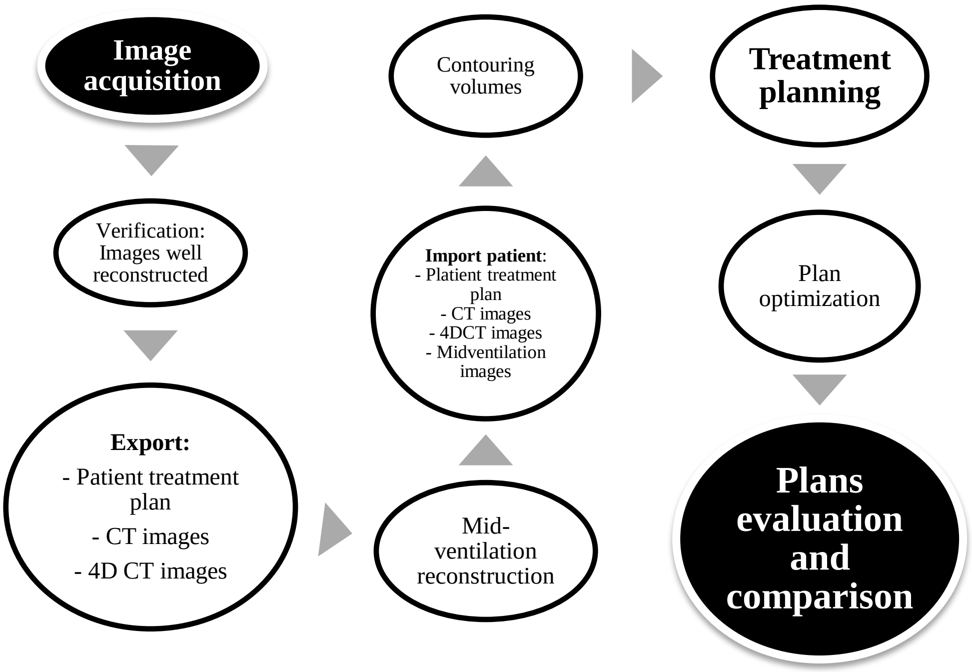

Fig. 1 - **Research process:** steps for all patients

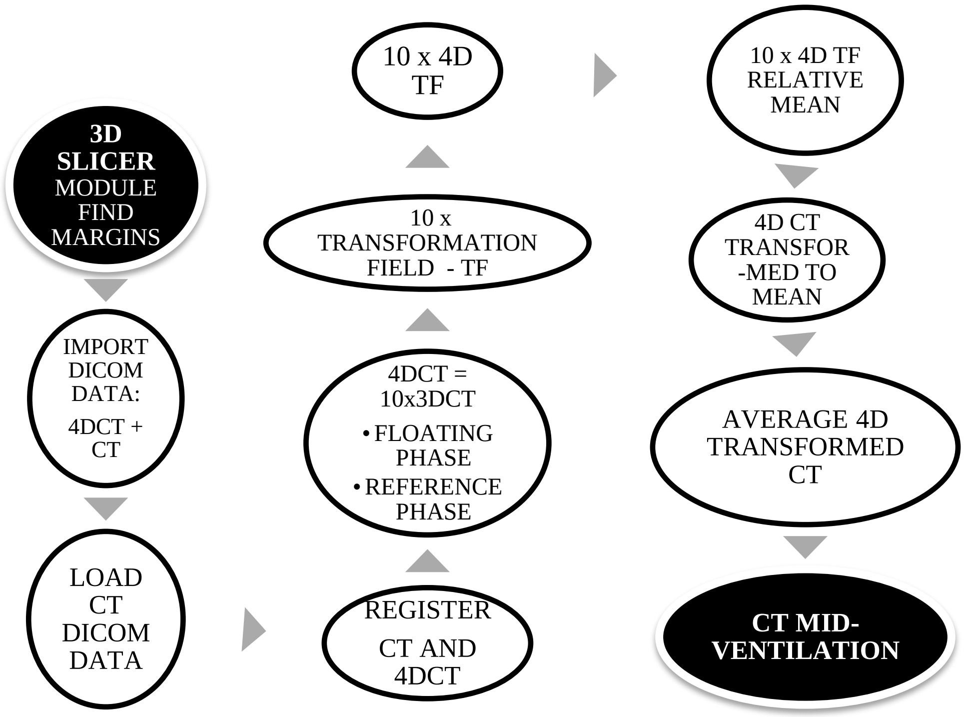

Fig. 2 - Mid-ventilation reconstruction process

Table 1 - Organs at risk contoured for each patient

Patient	Location	OAR	
1	Metastasis in RSL – 3 lesions	- Right Lung - Left Lung - Total Lung volume (R+L) - Spinal cord - Large Airways (R+L) - Small airways (R) - Trachea	- Heart - Aorta - Esophagus - Great vessels - Thoracic wall - Brachial plexus - Humerus (only for patient2)
2	Metastasis in RSL		
3	RSL with local invasion		
4	RML		

*RSL = right superior lobe; RML= right middle lobe.

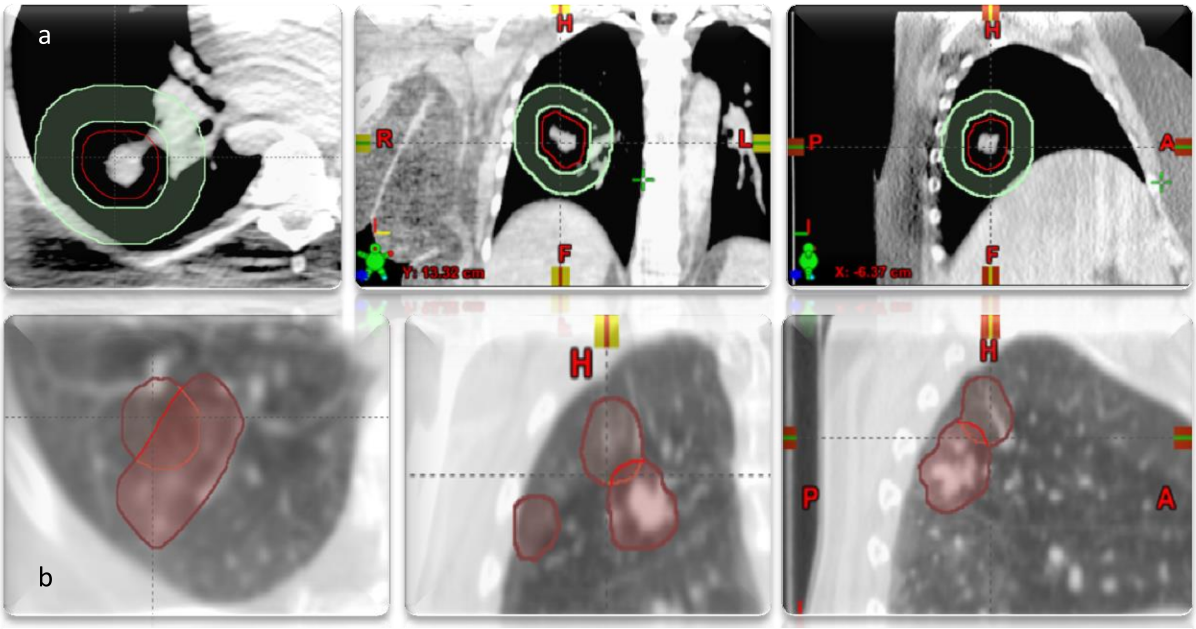

Fig. 3 - Contouring - a) Ring **b)** PTVcal: the sum of PTV1, PTV2 and PTV3

Table 2 - SBRT dose tolerance limits (Timmerman, 2011)[27]

Organ	Vol. (cc)	Vol. Limit (Gy)	Max Limit (Gy)
Aorta and major vessels	10 cc	31 Gy	37 Gy
Brachial Plexus	3 cc	14 Gy	17.5 Gy
Esophagus	5 cc	11.9 Gy	15.4 Gy
Heart	15 cc	16 Gy	22 Gy
Lung (Right+Left)	1500 cc 1000 cc	7 Gy 7.4 Gy	
Ribs (Thoracic wall)	1 cc	22 Gy	30 Gy
Small airways	0.5 cc	12.4 Gy	13.3 Gy
Spinal Cord	0.35 cc 1.2 cc	10 Gy 7 Gy	14 Gy
Trachea	4 cc	10.5 Gy	20.2 Gy

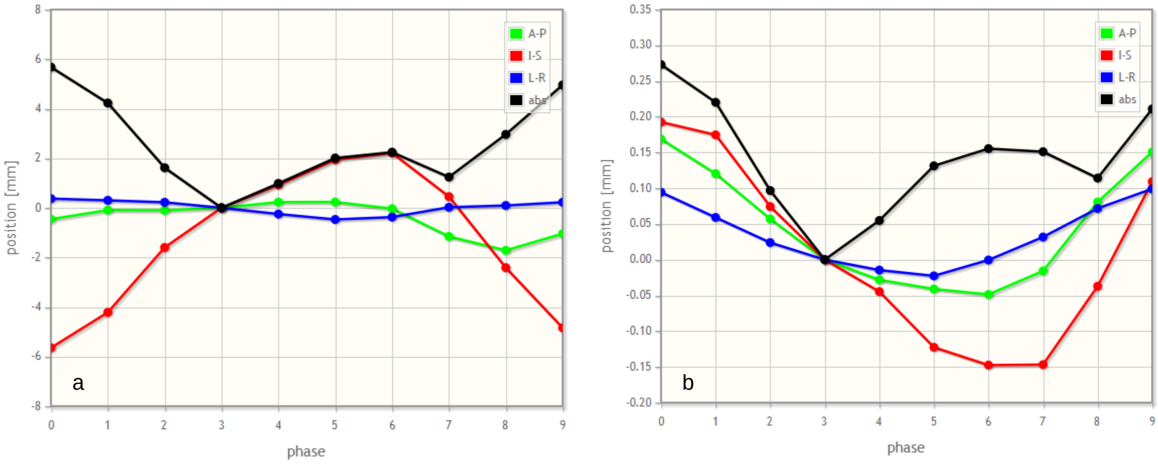

Fig. 4 - Target position in each respiratory phase in L-R (left-right), I-S (inferior-superior) and A-P (anterior-posterior) directions **a)** arms up **b)** arms down

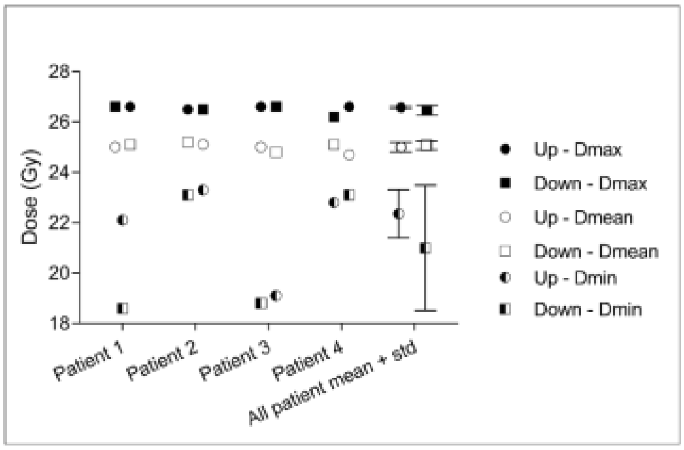

Fig. 5- Dmax, Dmean and Dmin for each patient and all patient mean doses

Table 3 – Mean and standard desviation (sd) values for the percentage of lung volume receiving x Gy.

Lung	Mean (sd)		
	Arms up	Arms down	*p-value*
V_{10Gy}	13.3 (9.1)	14.35 (9.48)	0.593
V_{15Gy}	7.98 (6.47)	8.83 (6.16)	1
V_{20Gy}	4.48 (3.33)	5.1 (3.5)	0.285

Table 4 – Total of monitor units

UM	Arms up	Arms down	p-value
Patient 1	13701	8118	n.a
Patient 2	10228	8522	
Patient 3	8000	8784	
Patient 4	12774	6334	
Mean (sd)	11 175.75 (2 576.49)	7 939.5 (1 104.84)	0.144

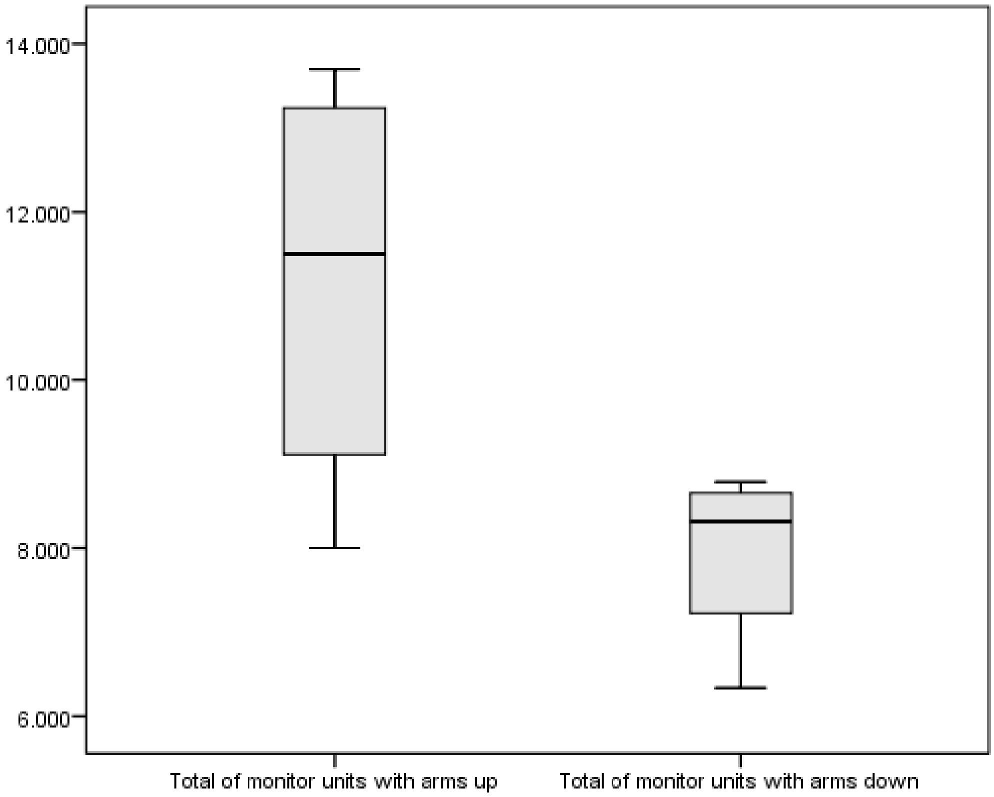

Fig. 6 - Total of monitor units: the variability of data

Conclusão geral

O posicionamento do doente deve ser um compromisso entre o conforto do doente e um posicionamento reprodutível para o tratamento, se este compromisso não for exequível a precisão do tratamento pode ser posta em causa devido ao aumento de erros de *set up*. O posicionamento pode ser feito com ou sem dispositivos de imobilização rígidos. A sua escolha deve ser feita tendo em conta o tipo de imagem/tecnologia disponível na sala de tratamento. A SBRT impõe um posicionamento com elevada precisão, respeitando sempre as co-morbilidades e o conforto do doente de forma a ser um posicionamento estável e reprodutível. Em alguns doentes o posicionamento com os braços para baixo pode ser vantajoso por diminuir a amplitude do movimento respiratório e consequentemente o volume a irradiar - PTV. Não foram encontradas diferenças estatisticamente significativas entre as variáveis em estudo, apesar disso, são notórias as diferenças nos valores das unidades monitor que se podem justificar com o facto do planeamento com os braços para cima ser feito sempre em primeiro lugar. Existe também uma diferença perceptível na variável do volume que recebe x Gy que tem valores inferiores no posicionamento com os braços para cima. Existe também uma ligeira diferença no volume do pulmão, sendo os valores inferiorescom os braços ao longo do corpo. Assim, pode concluir-se que a posição dos braços deve ser um compromisso entre a amplitude respiratória que o posicionamento provoca, as co-morbilidades do doente e entre o facto de irradiar mais tecido são com os braços para baixo.

Para futuros projetos e na mesma linha de investigação poderia estudar-se o impacto da variação da amplitude do movimento tumoral com os diferentes posicionamentos. Esta pragmática pode ser aplicada a patologias que variem com o movimento respiratório, como por exemplo, tumores de fígado.