INSTITUTO POLITÉCNICO DE LISBOA
ESCOLA SUPERIOR DE TECNOLOGIA DA SAÚDE DE LISBOA

UNIVERSIDADE DO ALGARVE
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Efeito da utilização da técnica de SGRT (Surface Guided Radiation Therapy) na redução dos erros Inter e Intra fração em tratamentos SBRT (Stereotactic Body Radiation Therapy) do pulmão

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Mestrado em Gestão e Avaliação de Tecnologias em Saúde

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“Nothing in life is to be feared.
It is only to be understood.
Now is the time to understand more,
so that we may fear less."
(Marie Curie)

Resumo

Introdução: Os doentes com cancro de pulmão tratados com *Stereotactic Body Radiation Therapy* exigem rigor no posicionamento e correspondência dos volumes alvo e órgãos de risco devido ao uso de doses de radiação elevada, com margens estreitas. Acresce considerar o ciclo respiratório, que por implicar movimento acarreta incertezas geométricas e dosimétricas. Com a técnica de *Surface Guided Radiation Therapy* é possível, sem o recurso a radiação ionizante, monitorizar em tempo real a posição do doente resultando potencialmente na minimização de erros interfração e intrafração.

Objetivo: Analisar o efeito da utilização de um sistema de *Surface Guided Radiation Therapy* na diminuição de erros e aumento da segurança do doente.

Metodologia: Foram elaborados dois artigos científicos com base em duas abordagens metodológicas distintas. O primeiro artigo corresponde a uma revisão sistemática da literatura que procura reunir a evidência existente sobre o tema, e o segundo, um estudo investigacional que pretende avaliar, em contexto clínico o contributo de um sistema de *Surface Guided Radiation Therapy* na redução de erros e aumento de segurança para o doente.

Resultados e Discussão: Apesar da escassez de literatura que fundamenta esta temática, os resultados iniciais confirmam o benefício da utilização de *Surface Guided Radiation Therapy*. Verificou-se que os principais fatores que levam à existência dos erros, sobretudo intrafração foram detetados antecipadamente e, passíveis de serem corrigidos, contribuindo para uma maior segurança no tratamento do doente.

Conclusão: A implementação de um sistema de *Surface Guided Radiation Therapy*, ao melhorar a precisão do posicionamento, ao controlar o movimento intrafração, torna possível um tratamento com mais segurança (menor toxicidade) e com maior qualidade (precisão).

Palavras-Chave: *Stereotactic Body Radiation Therapy* (SBRT)*, Surface Guided Radiation Therapy* (SGRT), Erros Intrafração, Erros Interfração, Segurança do Doente.

Abstract

Introduction: Lung cancer patients treated with Stereotactic Body Radiation Therapy, due to higher doses of radiation and strict treatment margins, require greater rigour in patient positioning and correspondence of treatment volumes and organs at risk. It is necessary to take into consideration the respiratory cycle, which causes movement, and therefore entails geometric and dosimetric uncertainties. By using a Surface Guided Radiation Therapy system, it is possible, without the use of ionising radiation, to monitor the patient's position, in real time, reducing inter and intra fraction errors.

Objective: Analyse the effect of using a Surface Guided Radiation Therapy system in reducing errors and increasing patient safety.

Methodology: Two scientific studies were developed based on two different methodological approaches. The first article is a systematic review of the literature that aims to summarize the current evidence on this subject. The second article, an experimental study that analyses the contribution of the use of a Surface Guided Radiation Therapy system in reducing errors and increasing patient safety.

Results and Discussion: There is a lack of literature on this subject, however, preliminary results support the use of a Surface Guided Radiation Therapy system. With the experimental study, it was possible to verify that the factors that lead to the existence of errors, especially intrafraction ones, were detected in advance and could be corrected, thus contributing to greater safety in the treatment of the patients.

Conclusion: With the implementation of a Surface Guides Radiation Therapy system, by improving positioning accuracy, and controlling intrafraction motion, it is possible to make treatments safer and with higher quality.

Key Words: Stereotactic Body Radiation Therapy (SBRT), Surface Guided Radiation Therapy (SGRT), Intrafraction errors, Interfraction errors, Patient Safety

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Lista de Siglas e Abreviaturas

CBCT – *Cone Beam Computer Tomography*

CCC – Centro Clínico Champalimaud

CTV – *Clinical Treatment Volume*

DIBH – *Deep Inspiration Breath Hold*

IGRT – *Image Guided Radiation Therapy*

ITV – *Internal Target Volume*

LOA – *Limit of Agreement*

OAR - *Organs at Risk* / Orgaõs de Risco

OMS – Organização Mundial da Saúde

PTV – *Planning Treatment Volume*

SABR - *Stereotactic Ablative Radiotherapy*

SBRT – *Stereotactic Body Radiation Therapy*

SGRT – *Surface Guided Radiotherapy*

SRS – *Stereotactic Radiosurgery*

ROI – *Region of Interest*

RT – Radioterapia / *Radiotherapy*

Introdução Geral

Segundo o Registo Oncológico Nacional 2019, o cancro do pulmão foi o segundo cancro com maior incidência em Portugal, com 5208 novos casos nesse ano (32.2/100 000 pessoas-ano)[1]. A Organização Mundial de Saúde (OMS) estima que em 2020, em Portugal, foram diagnosticados 5415 novos casos de cancro do pulmão, representando a terceira neoplasia mais frequente no país, embora a primeira em termos de mortalidade[2].

A radioterapia (RT) é um tratamento eficaz no tratamento do cancro do pulmão. Para doentes de alto risco ou em que não é possível resseção cirúrgica, a RT é uma opção terapêutica adequada. Foi também demonstrado que a combinação quimio-radioterapia prolongou significativamente a taxa de sobrevida destes doentes[3]. Existe evidência que 53,6% dos casos de cancro do pulmão de pequenas células desenvolvem uma ou mais indicações para RT em algum momento no decurso da doença (45,4% no seu tratamento inicial, e 8,2% mais tarde para a recidiva ou progressão da doença). Quanto aos casos de cancro do pulmão de não pequenas células 64,3% dos casos requerem RT (45,9% no seu tratamento inicial e 18,3% mais tarde no decurso da doença). No total, 61,0% de todos os doentes com cancro do pulmão desenvolverão uma ou mais indicações para RT no seu tratamento inicial, e 16,5% casos na recidiva ou progressão da doença[4].

A complexidade de diagnóstico e tratamento do cancro do Pulmão suscita um crescente interesse nesta área e, consequentemente, o desenvolvimento de novas investigações.

Com o avanço da tecnologia em RT é possível a utilização da técnica de Stereotactic Body Radiation Therapy (SBRT) que pressupõe a administração de doses de radiação elevadas, hipofracionando a dose administrada recorrendo a planos dosimétricos altamente conformados[5]. Esta premissa exige maior rigor no posicionamento do doente, conseguido através de uma correspondência das estruturas anatómicas entre o plano de tratamento e a execução do mesmo. Para isto, geralmente, recorre-se à tecnologia *Cone-Beam CT* (CBCT)[6].

O aumento da complexidade dos tratamentos traduz-se no aumento dos riscos e erros associados. Um erro é uma conduta atípica, irregular ou inadequada, que resulta ou pode resultar em dano desnecessário para o doente[7,8]. O ineficaz posicionamento e os incorretos procedimentos de tratamento são alguns dos erros mais comuns em RT[9].

Nos tratamentos do cancro do pulmão é necessário ter em consideração o ciclo respiratório, que ao provocar movimento, acarreta incertezas geométricas e dosimétricas[10,11].

A utilização de sistemas de monitorização nos tratamentos de Radioterapia - *Surface Guided Radiotherapy* (SGRT) permite, através de câmaras instaladas na sala de tratamento que emitem uma luz infravermelha (e por isso sem recurso a radiação ionizante), monitorizar em

tempo real a posição do doente, comparando a sua superfície no momento do tratamento com o que foi planeado, permitindo a redução dos erros intrafração[12].

O sistema de SGRT é uma modalidade ótica que proporciona dados tridimensionais em tempo real para quantificar o desvio em relação à superfície de referência. Como resultado, pode proporcionar um controlo não invasivo de todo o processo de posicionamento e administração do tratamento. O seu uso não consegue fornecer uma visão da precisão da delimitação do volume de tratamento ou da distribuição de dose, mas pode alertar para potenciais fontes de erro relacionadas com a identificação e imobilização dos doentes, precisão, localização do isocentro ou do movimento do doente durante o tratamento[13]. Com a SGRT reduz-se também os erros intrafração, uma vez que o feixe de radiação é interrompido sempre que há um movimento superior à tolerância definida[14].

O protocolo de imagem, atualmente em vigor na Fundação Champalimaud para tratamentos de SBRT, é a aquisição de dois CBCT pré-tratamento para verificar o posicionamento do doente. O primeiro tem como intuito fazer um ajuste do posicionamento geral do doente e o segundo uma verificação mais pormenorizada da localização dos volumes de tratamento e órgãos de risco (OAR). Sempre que este último tenha desvios superiores a 2mm translacional e 1º de rotação, após a aplicação dos desvios repete-se novamente a aquisição do CBCT para confirmação final. Este protocolo foi definido de forma a garantir uma correta administração das elevadas doses de tratamento. Foi feita uma avaliação da dose adicional de radiação ionizante administrada por CBCT como forma de quantificar o acrescento de dose de radiação ionizante pela aquisição de múltiplos CBCTs. A dose administrada por CBCT é de 1,73±0,09mGy[15]. Com a implementação de um sistema de SGRT, ao melhorar a precisão do posicionamento, e controlando o movimento intrafração, é possível tornar o tratamento mais seguro e com maior qualidade[13].

Este trabalho será apresentado sob a forma de dois artigos. Um primeiro artigo de revisão sistemática da literatura, que tem como objetivo reunir a evidência atual sobre a utilização de sistemas de monitorização de superfície nos tratamentos de SBRT.

O segundo artigo, um estudo investigacional, tem como objetivo analisar o efeito da utilização de um sistema de SGRT na diminuição de erros e aumento da segurança do doente. Pretende-se avaliar o contributo do sistema SGRT para:

a) aumentar o rigor do posicionamento do doente;
b) reduzir o número de CBCTs adquiridos ao utilizar o SGRT para posicionar os doentes;
c) contabilizar as interrupções intrafração provocadas pelo movimento do doente;
d) identificar quantas interrupções intrafração não são momentâneas e que implicam a realização de novo CBCT para correção da posição;
e) quantificar os tempos totais de tratamento com e sem SGRT para avaliar a influência do tempo despendido com a sua utilização.

A realização deste estudo respeita os princípios éticos inerentes ao processo de investigação tais como: solicitar a autorização das instituições envolvidas e obter a aprovação da sua comissão de ética nomeadamente, Escola Superior de Tecnologia da Saúde de Lisboa (Anexo 1) e Fundação Champalimaud (Anexo 2); informar os participantes sobre a investigação, o seu processo e à divulgação dos resultados, pedir o seu consentimento (Apêndice 1) e garantir o direito ao anonimato e confidencialidade dos dados dos participantes[16].

Este formato foi o escolhido com o objetivo de futura publicação em revista científica e é considerado o mais adequado para a produção científica contribuindo assim para a disseminação do conhecimento.

SECÇÃO 1

The role of Surface Guidance in Stereotactic Body Radiation Therapy treatments – A systematic review

Nicolle Gomes[1,2,3], Nuno Pimentel[2], Margarida Eiras[3]

ABSTRACT

Introduction: Stereotactic Body Radiation Therapy delivers high doses of radiation, hypofractionating the treatment using highly conformed dosimetric plans, requiring greater accuracy in patient positioning. The use of a Surface Guided Radiotherapy system allows for real-time monitoring of patient's position, by comparing the patient surface at the time of treatment with what was planned, reducing intrafraction errors. There are several publications on the use of Surface Guided Radiotherapy in cranial Stereotactic Radiosurgery treatments, as well as on the use of a Deep Inspiration Breath-Hold approach in breast treatments. However, data is limited in its use for Stereotactic Body Radiation Therapy.

Objective: Summarize the current evidence on the use of surface guidance on Stereotactic Body Radiation Therapy.

Material and Methods: A systematic literature review was performed, based on an electronic search in PubMed, and Web of Science databases. The descriptors "SGRT, "surface guided", "SBRT", "SABR", "radiosurgery" and "Stereotactic Radiotherapy" were used, and studies based on clinical evidence included. All studies based on phantoms and related to quality assurance measures were excluded. Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses - PRISMA guidelines, five articles were selected for the review.

Results: Incorporating Surface Guidance into the clinical workflow for Stereotactic Radiotherapy reduces the amount of variation between setup in the treatment room and the final CBCT localization. It's a valuable tool for initial positioning serving as a substitute for KV imaging and there are fewer shifts when setting up the patient. It is effective in detecting intrafractional motion, without the use of ionizing radiation. The exact correlation between patient surface and the internal target motion is not yet known, so it is recommended to combine it with image guidance such as Cone Beam CT.

[1]Mercurius Health
[2]Fundação Champalimaud
[3]Escola Superior de Tecnologias da Saúde de Lisboa, Instituto Politécnico de Lisboa

Conclusion: The use of Surface guidance in stereotactic treatments is helpful in initial patient setup and a feasible approach for motion management and respiratory monitoring.

Keywords: SBRT, SABR, Radiosurgery, SGRT, Surface Guided

RESUMO

Introdução: A Radioterapia estereotáxica administra altas doses de radiação, hipofracionando o tratamento, com base em planos dosimétricos altamente ajustados, requerendo maior precisão no posicionamento do doente. A utilização de radioterapia guiada por superfície permite a monitorização em tempo real da posição do doente, comparando a superfície deste no momento do tratamento com a planeada, reduzindo os erros intrafração. Existem várias publicações sobre a utilização de sistemas de monitorização de superfície em tratamentos estereotaxicos cranianos, bem como sobre a utilização de uma abordagem de inspiração profunda nos tratamentos de mama. No entanto, a evidência sobre a sua utilização em tratamentos estereotaxicos é limitada.

Objetivo: Resumir a evidência atual sobre a utilização de sistemas de monitorização de superfície nos tratamentos de Radioterapia Estereotaxicos.

Materiais e Métodos: Foi realizada uma revisão sistemática da literatura, com base numa pesquisa eletrónica nas bases de dados *Pubmed* e *Web of Science*. Foram utilizados os descritores "SGRT, “surface guided”, "SBRT", “SABR”, “radiosurgery” and “Stereotactic Radiotherapy” e os artigos baseados em evidência clínica incluídos. Artigos baseados em estudos em fantomas e medidas de controlo de qualidade do sistema foram excluídos. Utilizando as *guidelines* da declaração Prisma (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*), cinco artigos foram selecionados para o corpus da análise.

Resultados: A incorporação da monitorização de Superfície no fluxo de trabalho clínico para tratamento de Radioterapia Esterotática reduz a variabilidade entre o posicionamento do doente na sala de tratamento e a localização final da imagem de verificação adquirida. É uma ferramenta útil para o posicionamento inicial como substituto da imagem KV e há menos desvios na posição do doente. É eficaz na deteção de movimento intrafração, sem o uso de radiação ionizante. A correlação exata entre a superfície do doente e o movimento do volume alvo interno ainda não é conhecida, pelo que se recomenda combiná-la com a utilização de imagens de verificação.

Conclusão: A utilização de SGRT para tratamentos estereotaxicos é útil no posicionamento inicial do doente e uma abordagem viável para a gestão do movimento e monitorização respiratória.

Palavras-Chave: SBRT, SABR, Radiocirugia, SGRT, Surface Guided

INTRODUCTION

The SBRT technique requires the delivery of high radiation, hypofractionating the treatment and using highly conformed dosimetric planes. This premise requires greater accuracy in patient positioning, through a correspondence of the anatomical structures between the treatment plan and its execution. Cone-Beam CT (CBCT) technology is generally used for this[1,2].

The use of Surface Guided Radiotherapy (SGRT) imaging systems, which use cameras installed in the treatment room that emit infrared light (and therefore without additional ionizing radiation), allows for real-time monitoring of the patient's position, comparing the patient's surface at the time of treatment with the planned one, thus reducing intrafraction errors[3,4].

There are several publications on the use of SGRT in cranial Stereotactic radiosurgery (SRS) treatments as well as on the use of a Deep inspiration Breath Hold (DIBH) approach in breast cancer treatments. The use of a technique in which breathing is monitored allows treatment to be administered only in the DIBH phase eliminating the uncertainty of respiratory movement[5]. However, there is not much data on its use in extra cranial SBRT treatments especially for treatment sites where the patient's respiratory motion plays an important role when administering the treatment, such as the lung and liver tumors[5,6].

OBJECTIVE

The aim of this study is to summarize the current evidence on the use of surface guidance on SBRT treatments.

MATERIAL AND METHODS

Literature search

The methodology applied was based on the PICO strategy[7] and the following question was defined as the guiding question of the search in this research process: What is the evidence on the use of SGRT in SBRT treatments? A systematic literature review was conducted based on the PRISMA statement[8].

The descriptors "SGRT, “surface guided”, "SBRT", “SABR”, “radiosurgery” and “Stereotactic Radiotherapy” were evaluated in the *Medical Subject Headings (MeSH)*

query platforms, only existing the term radiosurgery. However, due to the importance of the different terms to better define the search, it was decided to maintain the use of all. They were combined with the Boolean character "AND" and "OR" as follows:
[SGRT OR “surface guided”] AND ["SBRT" OR “SABR” OR “radiosurgery”].
No particular commercial system was the focus of the review and so was not included in the search criteria.
The search was conducted between November 1 and 25, 2022, using the PubMed and Web of Science databases.
All identified articles were then assessed by applying the predefined selection criteria.

Study Selection

The previously selected descriptors should appear in the title and/or abstract of the articles.

Inclusion Criteria / eligibility criteria

The following eligibility criteria was defined: language (English and/or Portuguese); articles available in full text and free of charge. All articles should be based on clinical evidence with the effects being analysed on actual patients.

Exclusion Criteria

Studies that only aim to evaluate dosimetrical impacts of the use of SGRT, that were performed based on phantom studies and that related to quality assurance measures of the SGRT systems were excluded.

Quality assessment

The articles were sorted through Mendeley Reference Manager (v.2.79.0) and all articles that were repeated in the different databases were excluded. All the identified titles and abstracts of the found articles during the search process were screened by the first author as well as by and independent reviewer. After reading the title and abstract all articles that that did not meet the protocol premises were discontinued methodically developing a reduction process as shown in Figure 1. The main reasons for not meeting the requirements were being a review article with no original data, not addressing the guiding question defined for the study and having an inadequate setting or intervention.

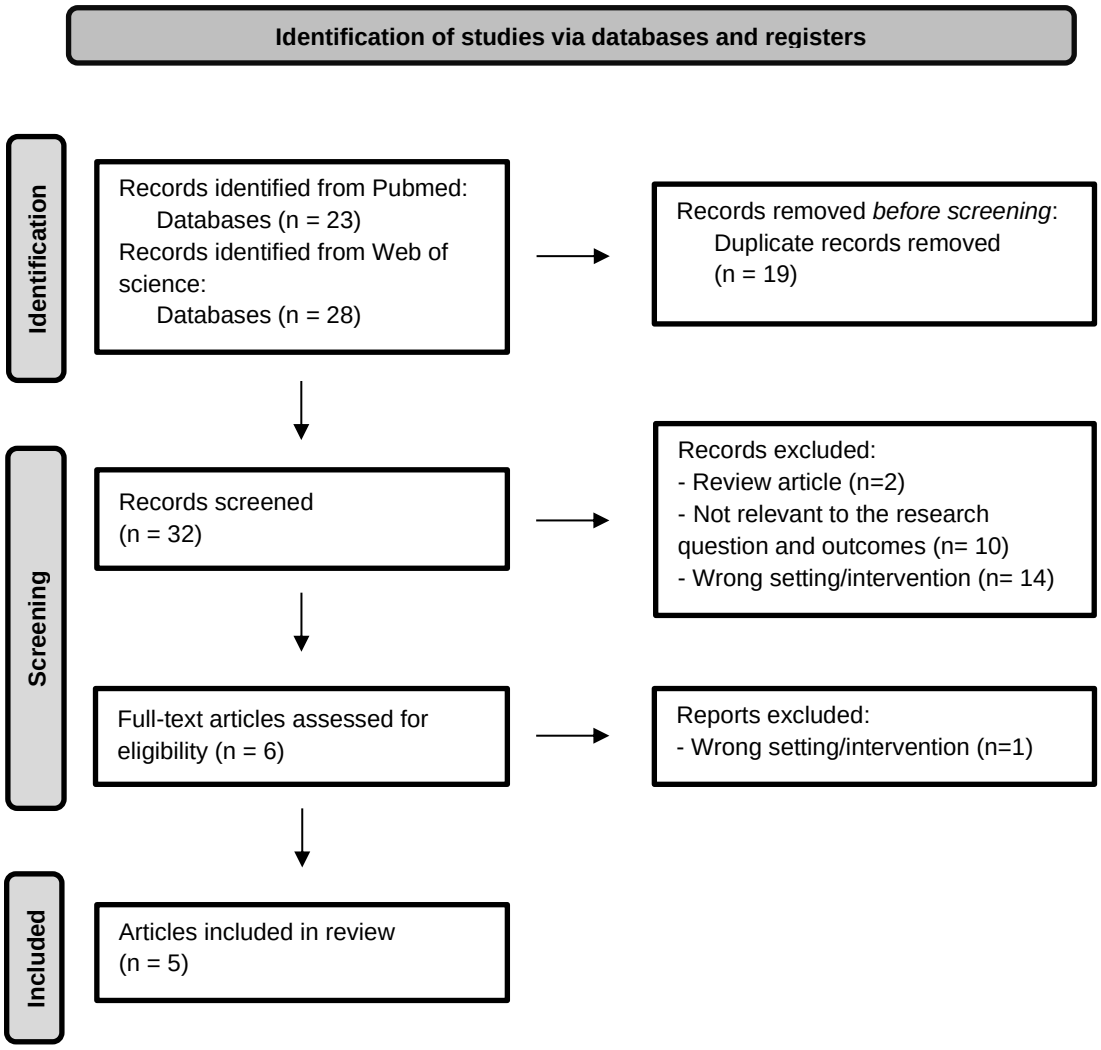

Figure 1: Prisma 2020 flow diagram of the selection process [9].

RESULTS

To ensure that the methodology of this study is understandable and transparent, Table 1 lists the five articles that made up the corpus of the research, their purpose, methods and main findings.

Table 1: Studies included in the systematic review their purpose, methods and results.

Titule	First Author	Purpose	Methods	Main Results
S1: Impact of use of optical surface imaging on initial patient setup for stereotactic body radiotherapy treatments[4]	Brian Leong	Verify the utility of using a SGRT technique for initial patient setup.	Comparison between two cohort groups: a) Non-SGRT: the patient was aligned through skin marks, shifted the couch to the treatment isocenter and acquired KV orthogonal bony anatomy correction and then a CBCT was acquired for final target localization. b) SGRT group: SGRT setup was introduced after the laser alignment and before the KV imaging.	The addition of SGRT into the clinical workflow for SBRT treatments reduces the magnitude of setup deviations between in-room setup and final CBCT localization.
S2: Use of surface-guided radiation therapy in combination with IGRT for setup and intrafraction motion monitoring during stereotactic body radiation therapy treatments of the lung and abdomen[10]	John H. Heinzerling	Quantify the accuracy of the SGRT system in positioning patient´s and also in detecting intrafraction motion during SBRT treatments	For inter fraction setup error evaluation each patient was alternately positioned using the SGRT system or, orthogonal planar kV imaging before a CBCT was acquired. For intra fraction motion evaluation SGRT continuously monitored the treatment.	SGRT is a valuable tool in the initial positioning in substitution of KV imaging prior to a CBCT. It is also effective in detecting intrafraction motion without the use of ionizing radiation and it may allow to consider treatment margins reduction.

S3: Feasibility of Optical Surface-Guidance for Position Verification and Monitoring of Stereotactic Body Radiotherapy in Deep-Inspiration Breath-Hold[11]	Patrick Naumann	Report the initial experience of combining SGRT and Image Guided Radiotherapy (IGRT) for patient positioning and treatment monitoring for SBRT of lung and liver using a DIBH approach	Lung and Liver patients treated with SBRT, using DIBH approach. DIBH reproducibility was validated in-room by the SGRT system, and then a CBCT (in DIBH) was acquired to verify positioning. Shifts were applied and an additional CBCT was obtained to validate reproducibility.	SGRT for lung and liver tumor, in DIBH, is feasible although daily imaging is necessary due to the high interactional variability, especially for liver SBRT.
S4: *Surface guided frameless positioning for lung stereotactic body radiation therapy*[12]	Sebastian Sarudis	Determine the feasibility in using a frameless immobilization device with aid of a SGRT system for SBRT treatments of the lung to verify Intra-fractional patient and tumor shift during the treatment delivery.	After patient setup (positioned in a half body sized vacuum cushion placed on a wingstep), orthogonal kV images were acquired, and shifts applied based on bony anatomy followed by a CBCT. The breathing amplitude gating window was defined to encompass the normal breathing cycle based on the 4DCT with an additional 1mm margin in all directions. The magnitude of the shifts was quantified and estimated the impact on the delivered dose.	The use of a simple immobilization device together with SGRT is a feasible approach for motion management and respiration monitoring for lung SBRT.

S5: Precision of image-guided spinal stereotactic ablative radiotherapy and impact of positioning variables[13]	Billiet Charlotte	Determine the accuracy of the SGRT system for spinal SABR treatments and also to verify different immobilization and positioning parameters.	SGRT system was used to set up the patient and to ensure their immobilization during treatment in 65% of the total amount of patients that took part in the study as the system was installed while the study was ongoing.	SGRT brings added value or patient monitoring during treatment as it allows for treatment interruption whenever necessary. This may permit the decreased use of immobilization devices enhancing patient comfort.

To analyse the impact of SGRT, while study 1 used the initial couch position after in room alignment and compared it to the couch position after final CBCT, study 2 had the CBCTs evaluated by the Radiation Oncologist and the shifts were recorded in order to determine setup errors[4,10].

After the CBCT evaluation in study 2, a gated reference (choosing the 50% amplitude of the breathing cycle) of the surface was acquired to be used continuously during treatment administration. The tolerances set were 2 mm for translational shifts and 1 mm for rotations. If patients were outside the defined tolerances for more than 2 seconds the treatment was stopped, and whenever this happened more than 3 times in one treatment, or exceeded 2 seconds, the CBCT was repeated[10].

During treatment delivery monitoring and despite using a DIBH approach the maximum error permitted in study 3 was slightly higher than in study 2. They allowed for 3mm and 2º for translational and rotational differences, respectively[11].

As for study 4 during the delivery of the treatment the beam was automatically stopped and 30sec no action was allowed for the patient to return within tolerances. If this did not occur, a new CBCT was acquired. Once the treatment was delivered a final CBCT was acquired to be compared to the initial one and analyse intrafraction motion. In cases were a shift larger than 2mm was observed, the impact on the dose to the organ at risk was assessed. The total treatment time was also recorded[12].

As for the results, study 1 and 4 had similar outcomes. In all translational directions there was a smaller range and median deviation when using SGRT in the workflow. The maximum deviations observed in the SGRT group were considerably smaller than in the non-SGRT group. The same behaviour was observed for rotational shifts[4].

Study 4 shows that most of the fractions registered a shift smaller than 2mm (96.4% of the fractions for vertical and lateral shifts and 97.8% for longitudinal)[12]. These finding weren't so evident in study 2. Besides the longitudinal shift there was no significant difference between both setup methods. Despite this, the results show that SGRT is an effective method for patient setup. It is comparable to kV imaging with the advantage that is does not use additional radiation exposure to the patient[10]. In Study 3 the use of SGRT permitted the initial couch shifts based on the first CBCT to be close to zero and the use of a DIBH technique allows for the reduction of the irradiated volume when compared to free breathing[11].

When focusing on the interfraction shifts observed during continuous treatment monitoring, study 2 reports that in 10% of the fractions there was motion greater than the tolerances[10]. As for study 4 the SGRT system interrupted the beam in 21% of the fractions but the patient returned to the required threshold and so none of them required repositioning. As for the respiratory motion, the patients breathing range extended outside the defined gating window

at least once in 54% of the fractions. There was no correlation found between the magnitude shifts of the patient and the total treatment time, patient age, body mass index or tumor volume and therefore found that the tendency for moving is individual and depends on each patient[12]. In study 5, the treatment was interrupted by the system in 24% of cases, leading to the acquisition of an extra CBCT and online position correction and only then continuing with the treatment[13]. The DIBH approach used in study 3 allows for a prediction on tumor motion in correlation with surface motion. It was found that liver targets have higher shifts when compared to lung. The highest interfractional variability was in the cranio-caudal direction and the lowest in the left-right direction. Both intra and inter fraction variability is larger in liver targets suggesting there is a better correlation of the patient´s surface in lung rather than in liver[11].

Study 2 also gives some insight in this correlation as they found the use of the SGRT system to be effective in detecting patient motion and this could be a surrogate to detect large displacement in lung patients and will facilitate the use of smaller PTV margins[10].

The only study that evaluated the dosimetric impact of the motion was study 4. When evaluating the impact of the dose to the organs at Risk (OARs) the difference between planned and delivered dose was less than 2.6% of the prescribed PTV dose with exception for the ribs in one patient. In only a single fraction was the visible tumor at the end of the CBCT acquisition found to be outside the ITV, which translated to decrease of 0.4 Gy of the $D_{98\%}$. With these results, it was found feasible to use a simple immobilization device and SGRT to monitor patient motion and respiration for SBRT of the lung. Since the patients had no abdominal compression plates to restrict the respiration and therefore tumor motion, the shifts observed for the tumor were larger than those observed for the patient. The SGRT system monitors the patient ‘s surface and therefore not able to conclude on the correlation between the surface monitoring and the actual tumor position. Using a SGRT system reduces the risk of irradiating the patient a different geometry than what was planned for and brings a quality improvement to the current practice[12]. The fact that the use of a SGRT system allows for treatment interruption, if necessary, one may consider eliminating the use of stricter immobilization devices providing more comfort for the patients[13].

As for study limitations, study 1 was retrospective and so it was impossible to estimate the time dispended for the initial setup with SGRT versus laser alignment alone. However, since the use of SGRT into the clinical workflow for SBRT treatments reduces the magnitude of setup deviations between in-room setup and final CBCT localization it would be reasonable to replace the laser alignment with the use of surface imaging [4]. In fact, none of the studies considered the time dispended for patient setup while using SGRT and, despite this not being a purpose of any of them, it would be interesting to know the impact it has on the clinical workflow.

Another limitation of study 1 is the absence of a 6DOF couch. Rotational corrections are made manually, shifting the patient´s position relative to the couch position and that is not reflected on the couch coordinates. Since this study analysed data from when the system had been recently acquired, the proficiency in setup was not uniform among radiation therapists and this fact should be considered in the data interpretation. This study does not analyse the use of the SGRT system for patient monitoring during treatment delivery so there is no indication in its impact on inter fraction errors[4]. On the other hand, studies 4 and 5 do not analyse the impact of the use of an SGRT system in patient setup despite using it for that purpose. It only refers to the impact on patient motion during the delivery of the treatment [13].

Although the different studies have variations between them, use different SGRT systems and present limitations, they all refer to the advantages of the use of a SGRT system for greater accuracy and safety in SBRT treatments.

CONCLUSION

The use of SGRT for patient setup and monitoring during the delivery of SBRT treatments is feasible and useful. As for setup of the patient, the shifts are smaller when compared to an approach without SGRT. One of the main advantages of the use of SGRT is that it is a system that does not use any additional ionizing radiation and so it allows for a continuous monitorization of the patient throughout the delivery of the treatment. However, since the exact correlation between patients surface and internal target motion is still not known the use of this technique alone is not an option and it is recommended to associate it with the use of image guidance such as CBCT acquisition.

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SECÇÃO 2

Effect of using the Surface Guided Radiation Therapy technique to reduce inter and intra fraction errors in Stereotactic Body Radiation Therapy treatments to the lung

Nicolle Gomes, Margarida Eiras, Nuno Pimentel

ABSTRACT

Introduction: Stereotactic Body Radiation Therapy (SBRT) technique assumes the administration of high radiation doses and hypofractionated schedules requiring greater accuracy in patient immobilization and positioning. The use of Surface Guided Radiotherapy (SGRT) imaging systems allows on-line matching and monitoring of the patient's surface, reducing intrafraction and interfraction errors. The objective of this study is to analyse the effect of using a Surface Guided system in the reduction of errors and increase in patient safety.

Methods: 10 Lung cancer patients, treated with SBRT, were randomly divided into 2 groups. In the first group, patient setup was performed based on the tattoos from the planning CT and the fixed lasers. In the second group, the setup workflow was complemented with the Align RT (Vision RT Ltd, London, UK, Version 6.3.235.1) postural video feature. Both groups then had a Cone Beam CT (CBCT) acquisition to verify the correct position. The shifts applied, number of CBCTs and overall treatment times were evaluated. In both groups the SGRT system continuously monitored the patient during treatment and the number of interruptions analysed.

Results and Discussion: Pre-treatment setup time for the group using SGRT was 90sec longer (average). CBCT analysis showed a smaller magnitude of shifts in the SGRT group, especially in the longitudinal direction where the average is 0.22mm compared to 0.59mm in the non-SGRT group. Treatment time was similar for both groups. Treatment interruptions were recorded 202 times and of those, 48.7% due to a longitudinal movement.

Conclusion: The combination IGRT and SGRT should be considered as standard practice and used in a complementary manner. Overall, SGRT can increase the safety of radiotherapy treatments by preventing serious errors.

Keywords: SBRT, SABR, SGRT, Surface Guided, Patient Safety

INTRODUCTION

The Stereotactic Body Radiation Therapy (SBRT) technique assumes the delivery of high doses of radiation, hypofractionated schedules and use of highly conformed dosimetric plans. This premise requires greater accuracy in patient positioning, through a correspondence of the anatomical structures between the treatment plan and its execution. Cone-Beam CT (CBCT) technology is generally used to assure this.[1,2]

When treating lung tumors, respiratory motion has an impact in treatment planning and delivery. Respiration is an involuntary physiological process that results in motion of the organs in thoracic and upper abdomen regions such as lungs, liver, pancreas oesophagus, and breast. Intra and inter fractional motion of tumor/target causes geometric and dosimetric uncertainties in the radiation therapy treatment delivery[3,4]. Dosimetric effect of respiration-induced intrafractional organ motion is an important aspect on safety and accuracy in treatment delivery and, if not accounted for, the tumor may be underdosed as well as normal tissue sparing be compromised. Therefore, a safety margin called the Internal Target Volume (ITV) is added to the Clinical Target Volume (CTV) which considers the motion of the target during the whole respiratory cycle[5] . A 4DCT scan is performed and a 4D software automatically sorts the images into several individual three-dimensional image sets, each representing the entire patient's anatomy during a single respiratory phase. The tumor and organ movement can then be visualized and used for determination of the ITV[4,5].

The use of Surface Guided Radiotherapy (SGRT) imaging systems, which use cameras installed in the treatment room that emit infrared light (and therefore without additional ionizing radiation), allows for real-time monitoring of the patient's position, comparing the patient's surface at the time of the treatment with the planned one, thus reducing intrafraction errors[6,7]. This is possible through the principle of triangulation, that can reconstruct a three-dimensional representation of the patient's surface that is related to the treatment coordinate system[8]. SGRT also reduces intrafraction errors[9], since during delivery any inconsistencies between the actual live surface and the reference surface can be detected in real-time and the beam is interrupted whenever there is a movement above a defined tolerance[6,8,10]. The increased complexity of treatments translates into increased risks and associated errors. An error is considered as an atypical, irregular, or inappropriate conduct that results or may result in unnecessary harm to the patient[11,12]. Inefficient positioning or incorrect treatment procedures can result in treatment to the wrong patient, wrong anatomical site, greater doses to normal tissues or lower doses than prescribed to the treatment site. These are some of the most common errors in Radiotherapy (RT) [13,14]. Due to the high complexity of planning and delivering the treatment and the input of different professional groups, the risk for adverse effects and near misses in RT is an important aspect and should be studied. Especially since current

practices are continually changing in response to new research and the introduction of new technologies[11]. The success of RT in terms of the probability of tumor control depends on accurate delivery of radiation dose to the intended target volume [13,14]. With the implementation of an SGRT system, by improving positioning accuracy, and controlling intrafraction motion, it is possible to make treatments safer and with higher quality[6].

The objective of this study is to analyse the effect of using a SGRT system in reducing interfraction and intrafraction errors therefore increasing patient safety. For interfraction errors, it aims to compare the number of CBCTs acquired in two groups of patients and verify if it is possible to reduce its frequency, while also aiming to evaluate the contribution of the SGRT system in increasing the accuracy of patient positioning. As for intrafraction errors, the aim is to quantify interruptions caused by patient movement and identify how many of these are not momentary and require a new CBCT to make corrections and adjustments. It also aims to quantify total treatment times, with and without the use of SGRT to verify how much more time is consumed by using the SGRT system for patient positioning.

METHODS

The population of this study includes lung cancer patients undergoing external radiotherapy, treated with an SBRT approach. The inclusion criteria were patients over 18 years of age with a diagnosis of lung tumor and the ability to understand and provide informed consent. This study includes 10 SBRT patients with a total of 33 treatment fractions, treated between September 2022 and January 2023 on the Varian EDGE (Varian, Palo Alto, California) linear accelerator with a 6DOF (degrees of freedom) table. The SGRT system used was the Align RT (Vision RT Ltd, London, UK, Version 6.3.235.1). Patients were scanned using a Philips Big Bore 4DCT Scan (Philips, Amsterdam, Netherlands) and the immobilization devices used for patient positioning were a VacQfix™ Vacuum with a ArmShuttle™ Elite (Qfix Avondale, PA), a Kneefix™ 3 (Civco Medical solutions, Radiotherapy) and a pressure Belt (Orfit solutions, Belgium) for abdominal compression (Fig.1) Dosimetric plans were calculated on Eclipse (Varian, Palo Alto, California) External Beam Planning system (version 15.6) using a VMAT technique. Treatment courses ranged from 1 to 8 fractions with total treatment doses of 24Gy to 55 Gy. Treatment sites included primary and metastatic cancers of the lung.

The study respected ethical principles, which included requesting the authorization of the institutions involved, informing the participants about the research, asking for their consent for data collection and ensuring data anonymity and confidentiality.

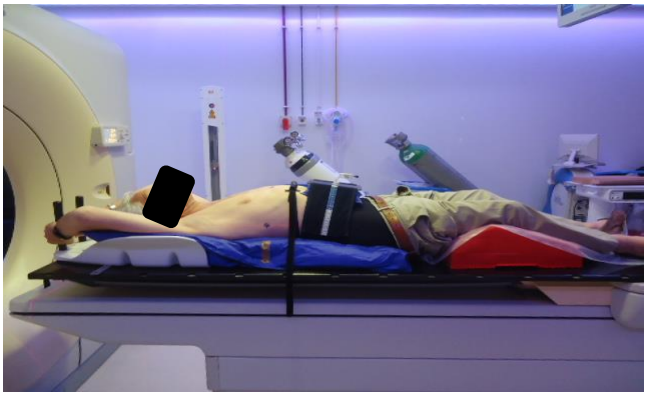

Figure 1: Immobilization devices used to setup patient

Inter Fraction error analysis

For this purpose, patients were randomly divided into two groups. The first group consisted of 5 patients (16 fractions) with patient setup performed based on the tattoos previously made in the planning CT and fixed laser beams present in the treatment room, according to the usual procedure of the institution. Once the patient was aligned, the table shifts to the isocenter were manually performed and the position verified with a CBCT acquisition. The second group consisted of 5 patients (17 fractions) with initial setup identical to the first and then complemented by using the Align RT postural video feature to confirm patients' position (with special emphasis in the patient's arms and shoulder position and body rotations). The shift to the treatment isocenter was performed automatically using the SGRT system that matches the live surface with the planning CT surface. Although the system allows for rotational corrections (Pitch, Roll and Yaw), it was decided not to correct these values and acquire the CBCT with no rotations to verify if there is an agreement between the values given by the SGRT system and the CBCT verification. The patient position was ultimately verified with a CBCT acquisition. For each treatment session, the CBCT was analysed by the Radiation Oncologist and the shifts were applied with no restrictions. These values were compared in both groups of patients to assess whether the group that used the SGRT system had smaller deviations (translating into a greater accuracy of positioning) when compared to the group that did not use the SGRT system. The number of CBCTs needed in each group for each treatment session was also determined to verify if the SGRT system allows for its reduction and consequently to a decrease of the dose delivered to the patient.

Once the CBCT was analysed and shifts applied a gated reference was acquired to be used continuously during treatment administration. The gated surface capture method acquires about 30 frames over a 6-second period, creating a graphical representation of the patient's breathing cycle within that time frame. Because it captures the patient's respiratory motion pattern it provides a more precise and reliable method for ensuring accurate patient positioning

during radiation therapy when compared to a normal reference capture. The reference point chosen for monitoring was the 50% amplitude of the breathing cycle [6,15].
The patient's setup time and actual treatment delivery time was recorded to evaluate the influence of using SGRT in the workflow.

Intra fraction error analysis

All patients in this study were assessed identically. The SGRT system continuously monitors the patient throughout the treatment. Every time the patient is out by the 3mm (translation) or 3º (rotation) threshold defined the treatment beam automatically stops. If the patient is out of tolerance momentarily and returns to baseline position the treatment will resume. If the patient goes out of tolerance and does not return to the initial position, the treatment is interrupted and a new CBCT is a acquired to adjust for the patient's new position (motion correction).

Data and Statistical Analysis

The total number of CBCTs acquired and the numerical values of the shifts applied were obtained using the Record & Verify Aria software (Varian, Palo Alto, California). To evaluate agreement of the rotational values obtained between each pair of methods (Align RT and CBCT), a Bland and Altman's graphical analysis was performed. A 95% limit of agreement (LOA) was used, recurring to the following equation:
LOA = (1.96 x SD) ± Mdif, where SD = standard deviation and Mdif = mean difference.
The Align RT system generates a CSV format report, per patient and treatment session that was used to quantify the number of interruptions that occurred. The analysis of total treatment times for each session was performed using the history tab in the ARIA Summary software (Varian, Palo Alto, California). As this option only accounts for the time from the beginning of the CBCT acquisition, a stopwatch was used to count the time from the moment the patient lays down on the treatment table, registering how long it took to setup each patient.
The data collected was statistically processed in Microsoft® Excel® for Microsoft 365 Version 2301 Build 16. 0. 16026. 20002 and IBM® SPSS Statistics Version 26.0 software (IBM Corporation, Armonk, New York).

RESULTS

Total Number of CBCT

The total number of CBCT required before starting the treatment delivery (Table 1) was in average 2,31 without SGRT and 2.06 with SGRT.

Table 1: Number of CBCT acquired prior to treatment delivery.

Nº CBCT	Minimum	Maximum	Mean
Without SGRT	2	3	**2.31**
With SGRT	2	3	**2.06**

Inter Fraction Errors - Patient Shifts

The results show a separate analysis for translations and rotations, since it was decided to only apply translational shifts automatically based on the Align Rt reading and not the rotational shifts.

Translational Shifts

Table 2 indicates the minimum, maximum, mean and standard deviation of the lateral, longitudinal and vertical shifts for both groups. The mean shift was not found to be significantly different for the lateral shift (0.28cm and 0.26cm without SGRT and with SGRT, respectively). The same is observed for the vertical shift (0.23cm and 0.29cm without SGRT and with SGRT, respectively). However, when we analyse the longitudinal shift, we see a bigger difference and the mean shift for patient's setup without SGRT is 0.60cm while with SGRT it is 0.26cm.

Table 2: Translational Shifts (cm).

		Minimum	Maximum	Mean	Std. Deviation
Without SGRT	Lateral Shift	.03	.83	**.28**	.21819
	Longitudinal Shift	.02	1.73	**.60**	.45076
	Vertical Shift	.01	.75	**.23**	.23249
With SGRT	Lateral Shift	.00	.57	**.26**	.18007
	Longitudinal Shift	.04	.72	**.26**	.19078
	Vertical Shift	.02	.50	**.29**	.16694

Figures 2, 3 and 4 provide a visual representation of the dataset for the lateral, longitudinal and vertical shift, respectively.

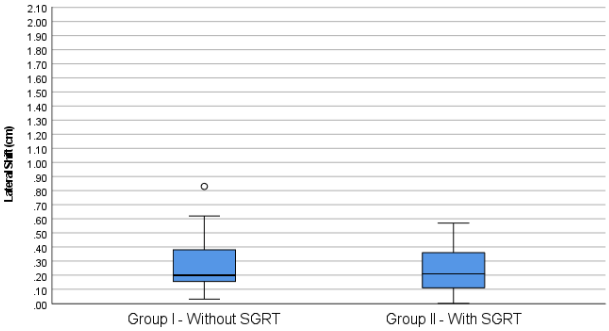

Figure 2: Lateral shift Boxplot (cm).

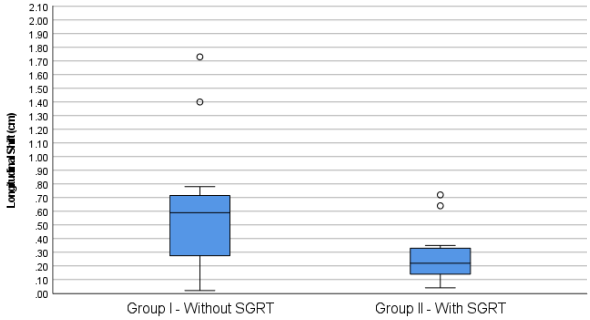

Figure 3: Longitudinal shift Boxplot (cm).

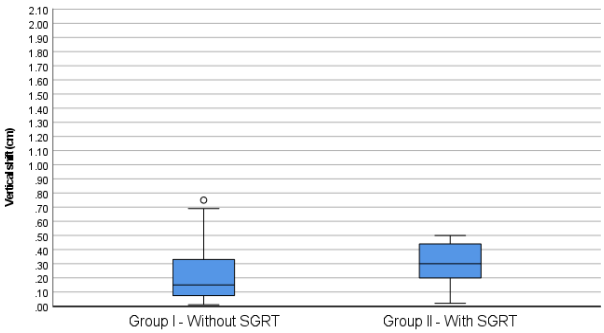

Figure 4: Vertical Shift Boxplot (cm).

Rotational Shifts

Table 3 indicates the minimum, maximum, mean and standard deviation of the rotational shifts (PITCH, ROLL, YAW) for both groups and the results are very similar between groups.

Table 3: Rotational Shifts (º).

		Minimum	Maximum	Mean	Std. Deviation
Without SGRT	PITCH	.1	2.3	**1.00**	.7576
	ROLL	.0	2.2	**.58**	.5745
	YAW	.0	1.7	**.80**	.4851
With SGRT	PITCH	.2	2.8	**1.27**	.7312
	ROLL	.0	2.5	**.73**	.6536
	YAW	.1	1.8	**.84**	.5533

The average shift indicated between both approaches was not found to be very different for any rotational directions. The rotational shifts given by the SGRT system were compared to the rotations seen on the CBCT and a Bland and Altman's graphical analysis performed to verify if both systems were in agreement.

Table 4 shows that the average for PITCH rotation was 1.14º (CBCT) compared to 1.22º (SGRT). The bland Altman Plot comparing the difference between the CBCT and the SGRT (Figure 5) shows a Bias of 1.1º. In 95% of the cases the difference between both systems are between 4.86º (UPL) and -2.67º (LLA).

Table 4: Comparison between CBCT and SGRT shifts for PITCH (cm).

	Minimum	Maximum	Mean	Std. Deviation
CBCT PITCH	.10	2.80	**1.14**	.74458
SGRT PITCH	.00	4.00	**1.22**	.88974

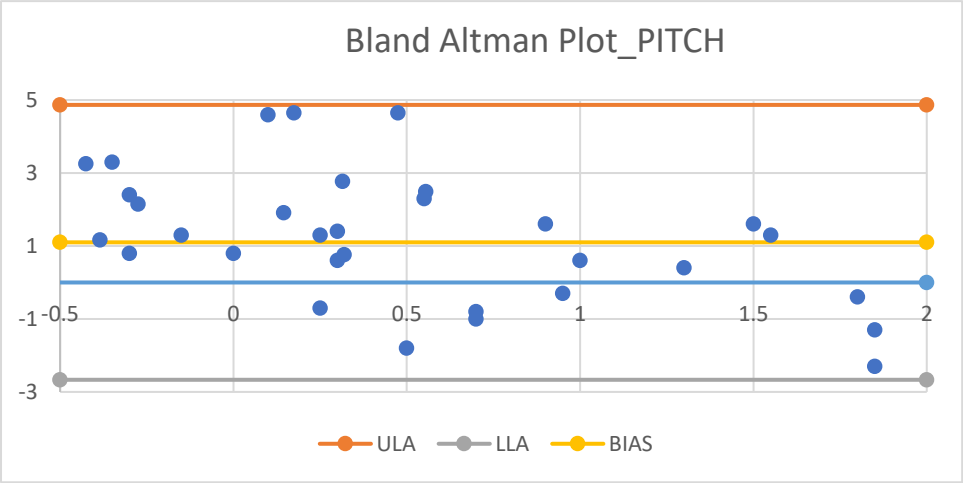

Figure 5: Bland Altman Plot for agreement in Rotational Shifts_PITCH (CBCT-SGRT)

As for the ROLL rotation the mean value is 1.07º for CBCT and 0.65º for SGRT (Table 5). The Bland Altman graph (Figure 6) shows a Bias of -0.09º. In 95% of the cases the difference between both systems are between 2.93º (UPL) and -3.11º (LLA).

Table 5: Comparison between CBCT and SGRT shifts for ROLL (cm).

	Minimum	Maximum	Mean	Std. Deviation
CBCT ROLL	.00	4.00	**1.07**	.93614
SGRT ROLL	.00	2.50	**.65**	.61191

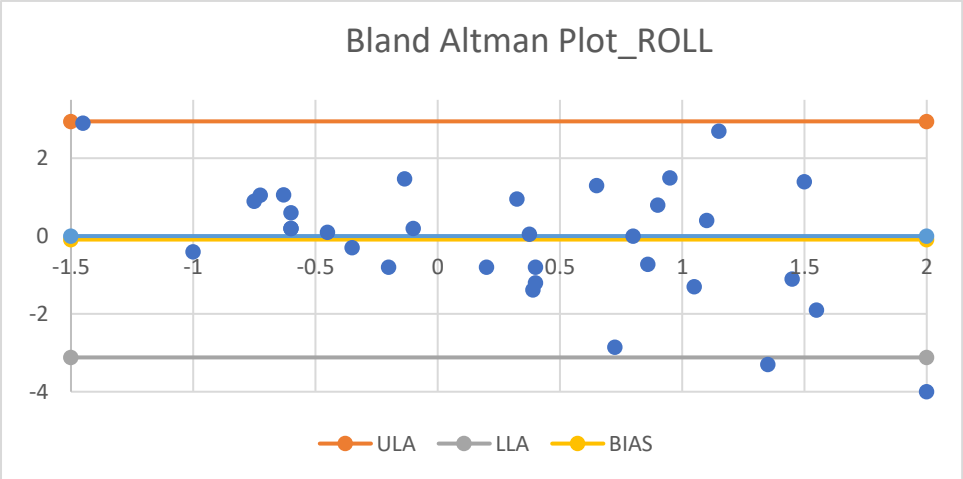

Figure 6: Bland Altman Plot for agreement in Rotational Shifts_ROLL (CBCT-SGRT)

When analysing the YAW direction (Table 6), the average shift was -0.06º (CBCT) and -0.44º (SGRT). The Bland Altman graph (Figure 7) shows a Bias of 0.38º. In 95% of the cases the difference between both systems are between 3.88º (UPL) and -3.12º (LLA).

Table 6: Comparison between CBCT and SGRT shifts for YAW (cm).

	Minimum	Maximum	Mean	Std. Deviation
CBCT YAW	.00	1.80	.82	.51342
SGRT YAW	.00	3.90	1.30	1.08735

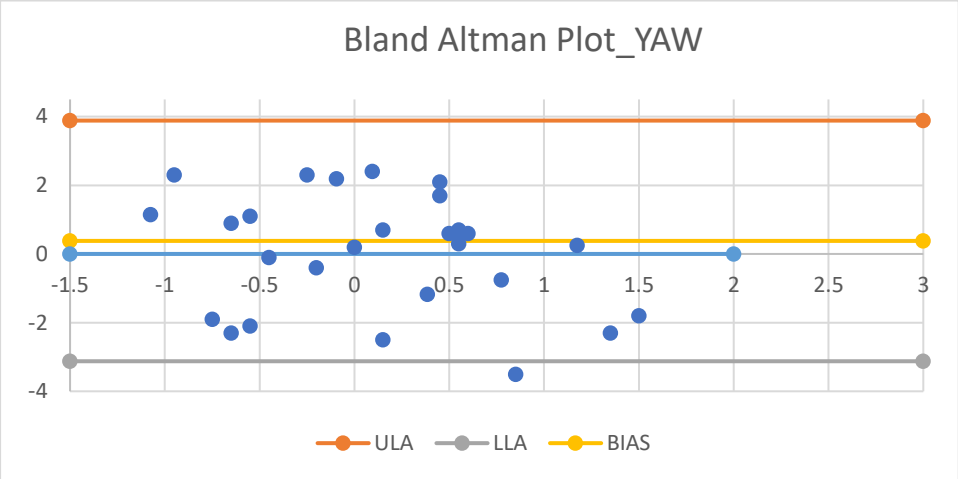

Figure 7: Bland Altman Plot for agreement in Rotational Shifts_YAW (CBCT-SGRT)

Intra fraction Errors - Treatment Interruptions

During the 33 fractions we were able to verify that the SGRT system interrupted the treatment beam 202 times. All patients had, in at least one fraction of their treatment, the SGRT system interrupting the beam. As seen on Table 7, the average time a patient was out of tolerance was 2.6sec. Although we have a minimum value of 0.10 seconds out of tolerance there was a case where the total time out of tolerance was 1min41sec (101.27sec).

Table 7: Time Out of Tolerance (sec).

	N	Minimum	Maximum	Mean	Std. Deviation
Time Out of Tolerance	202	**.10**	**101.27**	**2.6181**	8.11674

There were only 2 interruptions (0.99%) that led to the need to acquire a new CBCT as the patient moved from the setup position, which needed to be corrected.

As presented on Figure 8 almost half of the patient's movement (48.7%) is in the longitudinal axis.

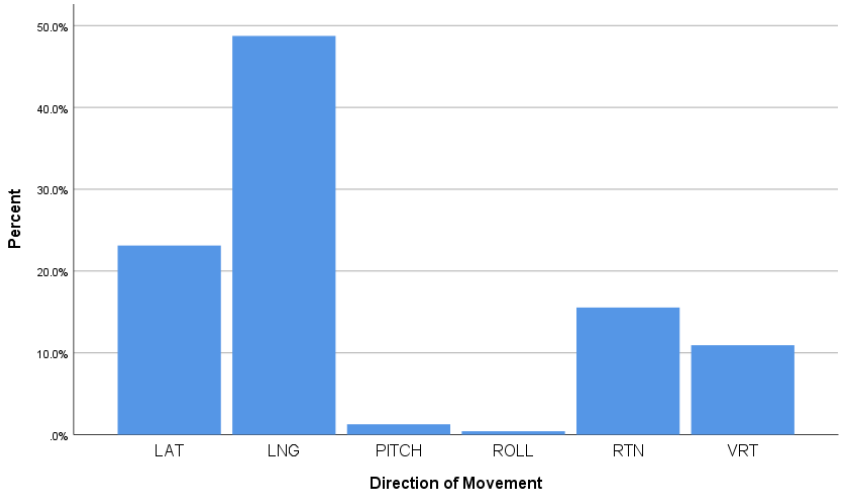

Figure 8: Percentage of Patient movement by direction.

Regarding the magnitude of the patients movement (Table 8), the average value was 3.96mm, minimum 3.03mm and maximum 9.88mm.

Table 8: Shift Magnitude (mm).

	Minimum	Maximum	Mean	Std. Deviation
Magnitude	**3.03**	**9.88**	**3.96**	.94488

When analysing the magnitude of the movement independently for each direction (Figure 9)

the longitudinal direction is slightly, but not significantly higher than the remaining directions.

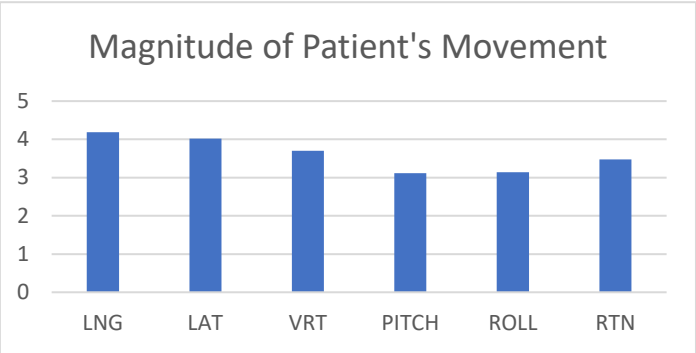

Figure 9: Magnitude of Patients Movement, by direction (cm/º).

Treatment Times

Treatment times (Table 9) are very similar in both groups. Actual treatment delivery time was on average 13min02sec for the group without SGRT and 12min26sec for the group with SGRT.

Table 9: Treatment Times (mm:ss).

Treatment Times (mm:ss)	Minimum	Maximum	Mean	Std. Deviation
Without SGRT	09:43	20:15	**13:02**	02:52
With SGRT	08:50	21:24	**12:26**	03:05

As for the time it takes to setup the patient (Table 10), there were slight differences. The mean time without SGRT for the 16 fractions was 4min03sec. The group with SGRT has an increase in patient setup close to a minute and a half, bringing the mean time for the 17 fractions to 5min35sec.

Table 10: Patient Setup Times (min:sec).

Patient Setup Time	Minimum	Maximum	Mean	Std. Deviation
Without SGRT	02:00	09:23	**04:03**	01:38
With SGRT	04:27	07:28	**05:35**	00:53

DISCUSSION

There was no significant difference between the number of CBCTs when comparing the positioning with or without the SGRT system. Despite using the SGRT system for patient setup it did not reduce the amount of CBCTs acquired prior to treatment delivery as initially expected. The exact correlation between the patient's surface and the internal motion of the tumor is not yet known and so we found the need to maintain at least both CBCTs (as departmental guidelines) to confirm patient position and especially to verify treatment volumes and OAR's.
As anticipated, there were no major lateral deviations or noticeable differences between both groups when examining the shifts detected on the CBCT. This is a result of the immobilization device used. The patients are positioned using a vacuum cushion that is moulded specifically to each individual patient that does not allow for major lateral displacements. While the vacuum cushion enables a relatively precise lateral position, it may not provide the same level of accuracy in the longitudinal direction. As a result, the patient's cranio-caudal position could differ slightly from the intended position. The results confirm that the longitudinal shifts were smaller and with fewer variations in the group setup up with SGRT. These findings show one of the biggest advantages of positioning the patient with the use of the SGRT system as it corrected for these shifts. Regarding the vertical shift it is mostly influenced by the patient's respiratory motion, and contrarily as to what was expected the group positioned using SGRT had higher shifts although the range of the actual shifts were lower and there were no outliers as opposed to the group without SGRT. When shifts are applied automatically by the SGRT system, they refer to a specific moment in time and therefore in the patients breathing cycle. The CBCT takes 1 minute to acquire an image and so the patient's breathing cycle is accounted for. For this reason, the motion seen in the treatment volume caused by the patient's breathing cycle might not translate to the motion seen on the patient's surface, especially when the tumor has a more posterior localization[4]. The vertical shift is not a good indicator to study the impact of the use of SGRT. However, further research is required to assess this finding.
Since there was no difference on the assessment of rotations for both groups, when looking at

the average shifts seen on the CBCT, it was noted that they were very similar between groups. As for the agreement seen on Bland-Altman graph, when analysing the difference between CBCT and the SGRT system we were able to verify that for PITCH and YAW rotations the bias was positive (1,1º and 0.37º, respectively) indicating that, in average, the shifts shown on the CBCT are slightly higher than on the SGRT. For the ROLL direction the opposite occurs as the bias is negative (-0.09º). The limits of agreement indicate that in 95% of the cases the differences between the measurements of both systems are between 4.87 º and -2.67º (PITCH); 2.93º and -3.11º (ROLL) and 3.88º and -3.12 (YAW). There is a high variability between these values that could be related to the fact that there is not a known correspondence between patient surface and internal position of the tumor. It would be relevant to increase the data input to confirm the absence of a bias and investigate its potential impact on the results and interpretation of the data.

As for the interfraction errors, during the 202 interruptions observed the use of the SGRT system prevented the patient being treated out of tolerance. Most of the interruptions were momentary and the patients did return to initial position allowing for the treatment to continue. These interruptions were mainly caused by the patients breathing pattern, which we could verify by analysing the direction in which the movements were observed. The treatment of lung patients is highly influenced by the respiratory motion and the longitudinal direction is where the biggest variations are mostly seen[16,17]. Just like observed on the shifts applied to the patient after analysing the CBCT these results also confirmed the longitudinal axis is the most influenced and so it indicates that the use of the SGRT system could help to mitigate this factor, hence making the treatment more accurate and safer. Pitch and Roll rotational shifts are rare, once again, most likely because the patient is moulded in to the vacuum cushion. This confirms that the immobilization devices used for these treatments allow for the patients comfort and are reproducible and therefore there is no need for more stricter devices. When analysing the magnitude of the patient's movement, since the threshold defined as tolerance to interrupt the treatment was 3mm, any value over this was taken into account and therefore the minimum shift observed was 3.03mm. The maximum shift registered was 9.88mm. An extremely high value when considering the conformity necessary for these treatments and high doses that are being delivered.

Actual treatment delivery times are very similar in both groups, and this was excepted as the procedure used for the treatment was the same. SGRT was continuously monitoring both groups throughout the treatment and automatically stopped when the patient was out of tolerance. When analysing the time it takes to setup the patient, the minimum setup time required for a treatment fraction without SGRT took as little as 2min while with SGRT the minimum time needed was 4min27sec. These results were also expected as the procedure of setting up a patient with SGRT requires more steps and so will naturally take longer. The use

of SGRT improves the overall safety and precision of the treatment as gross initial positioning errors are avoided[18]. When using SGRT to setup the patient the magnitude of the shifts seen on the CBCT are smaller than when compared to those seen on the group setup without SGRT. Despite this, the number of CBCT acquired prior to treatment were very similar in both groups (2 CBCTs). This relates to the fact that the exact correlation between the patient's surface and the movement of the internal target is still unknown therefore the use of this technique alone is not an option, and it is necessary to associate it with an imaging verification such as CBCT acquisition. The process of matching SBRT patients demands extra care and attention, which can be time-consuming. The longer the evaluation and image matching takes, the greater the possibility patient displacement from the original position. By using SGRT to monitor the patient throughout CBCT acquisition and evaluation, the confidence in patient position stability is increased[6]. The use of SGRT does not directly influence treatment times but it does increase in average 1min 30 sec the patient's setup time. We consider this not to be a disadvantage as the increase on time translates to a more accurate and precise patient setup and it does not compromise the current workflow.

The main advantage verified was the possibility of treatment interruption when the patient was not in the correct position. Because SGRT allows for real time intrafraction monitoring we were able to stop treatment delivery every time patients were out of threshold reducing the errors associated essentially to the patients breathing range.[16]

A limitation of surface-based systems is that it can be influenced by the gantry position blocking the cameras and giving a wrong reading. To prevent this and reduce uncertainties as whether it is a camera blocking or an actual patient movement, it is important to access an appropriate region of interest (ROI) as this is manually selected and influences the quality of the setup and monitoring. It is important to select a ROI that englobes the isocenter as well as both sides of the patient (especially for rotation detections). Another limitation of the system is that it only images the external surface of the patient, and correlation with internal anatomy remains uncertain thus needing more investigation in this aspect [6].

As for this study the main limitation was the reduced number of patients included due to time limits, and so patient recruitment will continue in order to achieve a bigger database and solidify the results. For future perspectives it would be recommended to study the possible correlation between surface motion and internal anatomy. Another future perspective is to correlate the motion seen on the 4DCT scan, analysing the patients breathing cycle and define the SGRT systems thresholds based on each individual patient's ITV instead of using a standard practice. The combination IGRT and SGRT should be considered as best practice and used in a complementary manner. Overall, SGRT can increase the safety of radiotherapy treatments by preventing serious errors.

CONCLUSION

The key technical advantages of SGRT systems are that they use non-ionizing radiation and provide near real-time monitoring. The visual information is intuitive and can improve patient safety.

The biggest advantage of the use of the system was the continuous monitoring of the patient during the treatment, allowing it to be interrupted whenever the patient leaves the defined margins of tolerance.

With the use of an SGRT system, by improving positioning accuracy and controlling movement through a continuous monitorization of the patient, it is possible to reduce inter and intra fraction errors making the treatment safer, with less toxicity and with higher quality and accuracy. It is in our opinion a useful and valuable tool to be used in SBRT treatments of the lung and should be considered a standard practice.

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Conclusão Geral

A realização deste trabalho permitiu confirmar que a constante evolução da Radioterapia obriga a uma procura constante do saber e atualização dos conhecimentos.

Ao realizar a revisão sistemática foi possível verificar a pertinência deste assunto uma vez que existe pouca literatura sobre o mesmo.

A utilização de SGRT para o posicionamento e monitorização dos doentes em tratamentos de SBRT é viável e útil. Os desvios verificados são menores quando comparados com uma abordagem sem SGRT. Uma das principais vantagens da utilização de SGRT é que é um sistema que não utiliza qualquer radiação adicional, permitindo assim uma monitorização continua durante o decorrer do tratamento.

A realização do artigo referente ao estudo investigacional permitiu confirmar o descrito na literatura. Ao utilizar um sistema de SGRT os desvios observados são menores podendo no futuro considerar-se realizar menos CBCT e eventualmente diminuir margens do ITV. A grande vantagem do uso do sistema foi a monitorização continua do doente no decorrer do tratamento permitindo que este fosse interrompido sempre que o doente saia das margens de tolerância definidas.

Contudo, uma vez que ainda não se conhece a correlação exata entre a superfície do paciente e o movimento do alvo interno, o uso desta técnica por si só não é uma opção e é necessário associá-la a uma verificação por imagem tal como a aquisição de CBCT.

Com a implementação de um sistema de SGRT, ao melhorar a precisão do posicionamento, e controlando o movimento intrafração, é possível tornar o tratamento mais seguro, com menos toxicidade e com maior qualidade e precisão.

A utilização de uma técnica de SGRT tem um efeito positivo e é uma ferramenta útil nos tratamentos de SBRT de pulmão pois permite reduzir os erros inter e intra fração.

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Anexos

Anexo 1 – Autorização Comissão Ética ESTeSL

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CE-ESTeSL-Nº.48-2022 - Nicole Gomes

1 mensagem

Comissão Ética <conselhodeetica@estesl.ipl.pt> 19 de setembro de 2022 às 09:14
Para: nicollegomes3@gmail.com, Margarida Eiras <margarida.eiras@estesl.ipl.pt>, nuno.pimentel@fundacaochampalimaud.pt
Cc: mestrados mestrados <mestrados@estesl.ipl.pt>

REFERÊNCIA INTERNA DO PROETO: **CE-ESTeSL-Nº.48-2022 –** Nicolle Gomes
TÍTULO DO PROJETO: Efeito da utilização da técnica de SGRT (Surface Guided Radiation Therapy) na redução dos erros Inter e Intra fração em tratamentos SBRT (Stereotatic Body Radiation Therapy) do pulmão
Tipo de Projeto/Estudo: Investigação 2º ciclo
INVESTIGADOR/A RESPONSÁVEL: Nicole Cadinha Gomes
Equipa: Margarida Eiras; Nuno Pimentel
INSTITUIÇÃO PROMOTORA: Escola Superior de Tecnologia da Saúde do Instituto Politécnico de Lisboa
Instituição(ões) envolvidas: ESTeSL-IPL; Fundação Champalimaud

Exma. Senhora Professora Doutora Margarida Eiras
Exmo. Senhor Professor Doutor Nuno Pimentel
Exma. Senhora Dr.ª. Nicolle Gomes, estudante de mestrado

Após os esclarecimentos a Comissão de Ética da Escola Superior de Tecnologia da Saúde de Lisboa (CE-ESTeSL) decidiu por unanimidade a emissão de parecer favorável.

O presente parecer tem em consideração a versão submetida do projeto e demais documentação enviada. Eventuais alterações nestes documentos determinam a necessidade de revisão do presente parecer.

Lembramos que todos os estudos que envolvem a autorização dos participantes e a recolha de amostras e dados anonimizados e/ou codificados têm de cumprir com o estabelecido no Regulamento Geral sobre a Proteção de Dados de 27 de abril de 2016.

Por último, solicita-se que, ao abrigo do artº 19 da Lei 21/2014 de 16 de abril e do disposto no nº 23 da atual versão da Declaração de Helsínquia, seja dado conhecimento à CE-ESTeSL do relatório final, com as conclusões do estudo, bem como de eventuais alterações ao protocolo de investigação e demais informações tidas por relevantes. Aproveitamos ainda para desejar o maior sucesso no desenvolvimento deste trabalho.

Com os melhores cumprimentos,
Rute Borrego

Rute Borrego | Professora Adjunta
Presidente da Comissão de Ética

Av. D. João II, lote 4.69.01- Parque das Nações
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Anexo 2 – Autorização Comissão Ética Fundação Champalimaud

Fundação Champalimaud

Parecer Ético para a Fundação Champalimaud

Efeito da utilização da técnica de SGRT (Surface Guided Radiation Therapy) na redução dos erros Inter e Intra fração em tratamentos SBRT (Stereotatic Body Radiation Therapy) do pulmão

Avaliador: Mário Miguel Rosa

Data da discussão: 18-10-2022

Apreciação: Positiva final

Introdução

Trata-se de um estudo de utilização da técnica de Radioterapia (RT) orientada pela posição de marcadores à superfície do corpo para colmatar as deficiências decorrentes da técnica de RT estereotáctica.

Este estudo teve já aprovação intermédia em Julho de 2022, sendo solicitadas alterações ao protocolo do estudo nomeadamente as que decorrem da aplicação do RGPD e ao consentimento informado, com uma versão em Português. Não foi necessário efectuar alteração ao conteúdo do CI visto não ser necessário prolongar as sessões ou criar uma nova sessão de avaliação.

Pertinência do estudo clínico e da sua concepção

Avaliação dos benefícios e riscos previsíveis

Protocolo, incluindo os planos de divulgação do estudo

As alterações solicitadas foram todas executadas, pelo que o parecer final é positivo

Fundação D. Anna de Sommer Champalimaud e
Dr. Carlos Montez Champalimaud
Fundada por António Champalimaud

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Aptidão do investigador principal e dos restantes membros da equipa

Condições materiais e humanas necessárias à realização do estudo clínico

Montantes e modalidades de retribuição ou compensação eventuais dos investigadores e participantes nos estudos clínicos e os elementos pertinentes de qualquer contrato financeiro previsto entre o promotor e o centro de estudo clínico

Modalidades de recrutamento dos participantes

Situações de conflito de interesses por parte do promotor ou investigador envolvidos no estudo clínico

Prazo e condições de acompanhamento clínico dos participantes após a conclusão do estudo clínico e, quando aplicável, o prazo de presunção se superior a um ano

Procedimento de obtenção do consentimento informado, incluindo as informações a prestar aos participantes.

Para os estudos clínicos com intervenção, acresce (artº 16º, nº 7):

Brochura do investigador

Qualidade das investigações

Disposições sobre indemnização por danos patrimoniais e não patrimoniais, incluindo o dano morte, imputáveis ao estudo clínico

Seguros destinados a cobrir a responsabilidade do investigador e do promotor

Assinado por: **MÁRIO MIGUEL COELHO DA SILVA ROSA**
Num. de Identificação: 07268526
Data: 2022.10.31 00:54:25+00'00'

Fundamentação da realização do estudo clínico com intervenção em que participem menores ou maiores incapazes de prestar consentimento informado

Anexo:

Parecer Ético para a Fundação Champalimaud

Efeito da utilização da técnica de SGRT (Surface Guided Radiation Therapy) na redução dos erros Inter e Intra fração em tratamentos SBRT (Stereotatic Body Radiation Therapy) do pulmão

Avaliador: Mário Miguel Rosa

Data da discussão: 19-7-2022

Apreciação: Intermédia positiva

Introdução

Trata-se de um estudo de utilização da técnica de Radioterapia (RT) orientada pela posição de marcadores à superfície do corpo para colmatar as deficiências decorrentes da técnica de RT estereotáctica.

A escolha da melhor forma de irradiar os tecidos neoplásicos provocando uma destruição destes e poupando os tecidos sãos adjacentes é o objectivo de várias técnicas de RT. A RT estereotáctica orienta o feixe de radiação de modo a colimar no tumor. No entanto, em estruturas móveis como a caixa toráxica, a posição da zona a irradiar varia em cada ciclo respiratório, com pequenas variações com os batimentos cardíacos. Mesmo requerendo a irradiação em inspiração forçada, o ponto de inspiração varia consoante a fadiga e capacidade de o doente aguentar a suspensão respiratória, sendo frequente a variação da posição em que o se encontra o tumor, no momento de irradiar.

Quanto mais complexa é a forma de administrar a dose de radiação (número e duração das sessões, forma de irradiar) tanto mais fácil é errar e acumular erros, somando não conformidades que diminuem a eficácia terapêutica.

Uma abordagem que permite mitigar os erros mais grosseiros é a utilização da estereotaxia, conhecendo a densidade dos tecidos até ao tumor, através de TAC e medição da forma como a radiação atravessa os tecidos. Porém, dados os movimentos do tórax, é sempre incerto que se esteja a irradiar no local em que se programou o foco da RT. De modo a diminuir mais o risco na própria sessão seja no momento de disparo da RT seja entre disparos na mesma sessão, é possível monitorizar a posição do tumor com TAC (mas sempre com radiação adicional nos tecidos sãos) ou através de um método que relaciona os pontos da superfície do tórax com os tecidos no interior do tórax, quer sãos quer tumorais. Este método é não invasivo e não contempla o uso de radiação, o que permite a não administração do

feixe se a posição do corpo não é exactamente a requerida. A prática actual consiste na tatuagem de alguns pontos, que são controlados manualmente juntamente com os feixes de laser que permitem a colimação. O sistema SGRT permite usar não apenas os pontos tatuados, mas a superfície toráxica para conhecer com precisão a localização do tumor e se este se desvia do feixe.

Este estudo é prospectivo e procura comparar a técnica standard com a SGRT através de vários indicadores de qualidade do tratamento e marcadores indirectos de eficácia. Não está previsto o estudo de sobrevivência ou tempo pra progressão de doença.

Pertinência do estudo clínico e da sua concepção

Trata-se de um estudo interessante, que permitirá a demonstração da melhor mitigação do erro face ao padrão usado actualmente

Avaliação dos benefícios e riscos previsíveis

Há um potencial benefício na técnica nova, mas pode ocorrer à custa da necessidade de repetir ou prolongar as sessões. Esta discussão deste risco deve ser presente no consentimento informado, o que não acontece presentemente.

Protocolo, incluindo os planos de divulgação do estudo

O Protocolo está detalhado excepto a ausência do cálculo da dimensão da amostra, e não é referido tratar-se de um estudo piloto.

Aptidão do investigador principal e dos restantes membros da equipa

A equipa de investigação (técnica e corpo clínico) é competente para a realização do estudo.

Condições materiais e humanas necessárias à realização do estudo clínico

A FC e o Serviço de Radioterapia possuem as condições materiais e humanas necessárias à condução do estudo.

Montantes e modalidades de retribuição ou compensação eventuais dos investigadores e participantes nos estudos clínicos e os elementos pertinentes de qualquer contrato financeiro previsto entre o promotor e o centro de estudo clínico

N/A

Modalidades de recrutamento dos participantes

O estudo será proposto a todos os doentes da FC com cancro do pulmão propostos para RT externa.

Situações de conflito de interesses por parte do promotor ou investigador envolvidos no estudo clínico

N/A

Prazo e condições de acompanhamento clínico dos participantes após a conclusão do estudo clínico e, quando aplicável, o prazo de presunção se superior a um ano

N/A: trata-se de um estudo concorrente com o tratamento de RT, que termina no momento em que terminam as sessões de RT.

Procedimento de obtenção do consentimento informado, incluindo as informações a prestar aos participantes.

O consentimento submetido encontra-se em língua inglesa – embora tenha um capítulo com título em português "Custos e compensações", e com várias siglas no texto informativo.

Deve ser revisto, e apresentado o texto nas línguas em que estará disponível.

Além disso, o risco de prolongar as sessões e de porventura ser necessário agendar outro momento de administração de RT deve estar contemplado nos riscos do estudo.

Para os estudos clínicos com intervenção, acresce (artº 16º, nº 7):

N/A

Brochura do investigador

N/A

Qualidade das investigações

N/A

Disposições sobre indemnização por danos patrimoniais e não patrimoniais, incluindo o dano morte, imputáveis ao estudo clínico

N/A

Seguros destinados a cobrir a responsabilidade do investigador e do promotor

N/A

Fundamentação da realização do estudo clínico com intervenção em que participem menores ou maiores incapazes de prestar consentimento informado

N/A

Apêndices

Apêndice 1 – Consentimento Informado

Consentimento informada para a realização de SGRT (Surface Guided Radiation Therapy) nos tratamentos de Radioterapia do Pulmão.

Este formulário de consentimento informado é dirigido a doentes com tumores de pulmão com indicação para tratamento de Radioterapia no Centro Clínico Champalimaud e que aceitem participar no seguinte projeto de investigação:

"Efeito da utilização da técnica de SGRT (Surface Guided Radiation Therapy) na redução dos erros Inter e Intra fração em tratamentos SBRT (Stereotactic Body Radiation Therapy) do pulmão"

Investigadora Principal:
Nicolle Gomes
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Parte I: Informação aos participantes no estudo

A Radioterapia é usada para tratar tumores de pulmão fazendo uso de radiação de alta energia (raio-x) de maneira a destruir o tumor. Graças ao desenvolvimento tecnológicos, tal como a usa de imagem guiada e sistemas de monitorização de superfície em tempo real o tratamento é feito de maneira mais precisa e seguro pelo que esperamos uma menor incidência de erros inter e intra fração.

Objetivo do estudo

Este estudo tem como objetivo analisar o efeito da utilização de um sistema de SGRT na diminuição de erros e aumento de segurança para o doente.

Pretende-se avaliar o contributo do sistema SGRT para o aumento no rigor do posicionamento do doente diminuindo erros interfração e também avaliar interrupções intrafração provocadas pelo movimento.

Após a informação sobre o processo lhe ter sido transmitida, apresenta-se em seguida um resumo escrito das características deste estudo. Por favor, leia com atenção a informação constante neste documento. Se tiver dúvidas, por favor coloque-as ao médico Radioncologista ou ao investigador principal que lhe está a apresentar este estudo para que possam ser esclarecidas.

Tipo de intervenção

O estudo não altera o plano clínico e terapêutico previamente estabelecido. A sua participação consistirá na autorização para a recolha dos dados obtidos durante o seu tratamento com a utilização de um sistema de monitorização de superfície e que serão posteriormente usadas pela equipa de investigação para avaliação.

Seleção de participantes

Estamos a propor-lhe a participação neste estudo, por ser um doente com tumor de pulmão a ser tratado com radioterapia na nossa instituição.
A participação neste estudo é totalmente voluntária. A escolha de participar ou não neste estudo é totalmente sua. O facto de escolher ou não participar neste estudo não vai alterar a qualidade dos serviços e tratamentos que recebe. Caso escolha participar, poderá desistir a qualquer momento, bastando para isso informar o seu médico Radioncologista ou investigadora principal.

Procedimentos

Para participação no estudo ser-lhe-á proposto que durante as suas sessões de tratamento seja utilizado um sistema de monitorização adicional que não lhe trará nenhum prejuízo em termos clínicos. O seu tratamento irá decorrer de forma habitual e de acordo com os protocolos já utilizados pela instituição.
O seu seguimento enquadrar-se-á no seguimento habitual de doentes oncológicos realizado pela instituição.

Utilização de dados

Caso aceite participar, os dados obtidos referentes ao seu tratamento (imagens, desvios aplicados e tempos de tratamento) serão avaliadas pela equipa de investigação, no fim do tratamento de um modo *offline.* Os dados relativamente às diferenças obtidas com utilização de um sistema de SGRT serão analisados para avaliar a potencialidade da utilização do sistema e se essas diferenças serão ou não significativas, a nível clínico.

Riscos associados

Este estudo não envolve riscos e incómodos adicionais para os participantes. Não irá interferir de forma alguma com o seu tratamento e seguimento.

Custos e compensações

A sua participação neste estudo não terá quaisquer custos adicionais para si. Não lhe será dada nenhuma compensação, monetária ou outra, pela sua participação neste estudo.

Confidencialidade

Como toda a sua informação, os dados recolhidos durante este estudo são mantidos estritamente confidenciais. A informação recolhida será armazenada numa base de dados protegida e apenas acessível para a equipa de investigação.

Partilha de resultados

Os resultados do estudo poderão partilhados em forma de comunicações, reuniões científicas e/ou artigos publicados em revistas científicas, sempre de forma completamente anónima. Poderá solicitar os resultados do estudo ao seu médico Radioncologista ou ao Investigador Principal do estudo.

Contactos

Caso tenha alguma dúvida sobre este estudo, seja antes ou durante a sua participação,

ou mesmo após este ter terminado, contacte o seu médico Radioncologista ou o Investigador Principal.

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Declaração da pessoa responsável por obter o consentimento

Declaro ter explicado integralmente o estudo clínico ao participante ou ao seu Representante Legal Autorizado (RLA). Com base na minha avaliação e na avaliação do participante ou do seu Representante Legal Autorizado, o mesmo teve acesso a toda a informação, conhecimento dos riscos e benefícios e foi-lhe permitida a possibilidade de colocar questões, tendo sido devidamente clarificado, de forma a permitir uma decisão informada. A discussão conducente ao consentimento será documentada no registo clínico eletrónico do participante, sendo-lhe entregue uma cópia deste documento.

A Assinar e datar pelo médico/radioterapeuta responsável da obtenção do consentimento:

Nome (letras maiúsculas): _____

Assinatura: _____ Data (dia/mês/ano):_____

Declaração do Participante (ou do seu Representante Legal Autorizado, RLA)

Li este formulário com a descrição do estudo. A pessoa responsável por obter este consentimento explicou-me o estudo e respondeu às minhas perguntas de forma clara e satisfatória. Ao assinar este formulário de consentimento, concordo com o seguinte:

1. Participar voluntariamente neste estudo de investigação

2. Autorizar a utilização e divulgação da minha informação de saúde protegida e codificada aos membros da equipa de investigação deste estudo.

3. Receber uma cópia assinada deste formulário de consentimento.

A assinar e datar pelo participante do estudo ou representante legal autorizado (RLA):

Nome do participante (letra maiúscula):_____

Nome do RLA (se aplicável):_____

Assinatura:_____ Data(dia/mês/ano):_____

Parentesco do RLA com o participante (se aplicável):_____