Artigo Original

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Efficiency evaluation of a Commercial Software for Breast Cancer plus Lymph Nodes Radiotherapy Planning

Avaliação da Eficiência de um Software Comercial para Planejamento de Radioterapia de Câncer de Mama com Linfonodos

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Abstract

The emergence of automation tools to assist in the routine tasks of Radiation Therapy centers has become increasingly prominent in recent years, particularly in sites with a high incidence of cancer. Various commercial software solutions are available for automated treatment planning; among these, EZFluence from Radformation Inc. (New York, USA) stands out as a tool used for achieving dose homogeneity within the target tissue by generating sliding window or Field-in-Field Beams. Therefore, the objective of this study is to assess the efficiency gains associated with the implementation of the EZFluence tool in clinical practice. Two experienced physicists retrospectively manually planned treatment for ten patients, with breast cancer and eight patients with breast cancer and lymph node involvement. The time taken to create clinically acceptable plans was recorded. Additionally, the time taken to generate plans using EZFluence was documented. The treatment protocol adopted for this study consists of hypofractionation, with 40.05 Gy delivered in 15 fractions. The mean time required to generate treatment plans decreased from 15 minutes and 57 seconds ± 4 minutes and 11 seconds to 8 minutes and 40 seconds ± 2 minutes and 48 seconds for plans generated using EZFluence for breast cancer patients without lymph node involvement (p-value < 0.01) and from 23 minutes and 52 seconds ± 4 minutes and 47 seconds for manual planning to 15 minutes and 56 seconds ± 1 minute and 26 seconds for plans generated using EZFluence for breast cancer patients with lymph node involvement (p-value < 0.01). Furthermore, the dosimetric quality of the plans was found to be comparable, once all the manual and automatic plans were adjusted to meet clinical acceptability criteria. The use of EZFluence has been demonstrated to enhance planning efficiency while upholding the dosimetric quality of treatment plans.

Keywords: automated planning, radiation therapy, breast cancer, automation, lymph nodes

Resumo

O surgimento de ferramentas de automação para auxiliar nas tarefas rotineiras dos centros de Radioterapia tornou-se cada vez mais proeminente nos últimos anos, especialmente em sítios com alta incidência de câncer. Diversas soluções de softwares comerciais estão disponíveis para o planejamento de tratamento automatizado; entre elas, EZFluence da Radformation Inc. (Nova York, EUA) destaca-se como uma ferramenta utilizada para homogeneizar a dose no alvo, gerando feixes de janela deslizante ou Field-in-Field. Portanto, o objetivo deste estudo é avaliar os ganhos de eficiência associados à implementação da ferramenta EZFluence na prática clínica. Dois físicos experientes planejaram manualmente retrospectivamente o tratamento para dez pacientes com câncer de mama e oito pacientes com câncer de mama com envolvimento linfonodal. O tempo necessário para criar planos clinicamente aceitáveis foi registrado. Além disso, o tempo necessário para gerar planos utilizando o EZFluence foi documentado. O protocolo de tratamento adotado para este estudo consiste em hipofracionamento, com 40,05 Gy em 15 frações. O tempo médio necessário para gerar planos de tratamento diminuiu de 15 minutos e 57 segundos ± 4 minutos e 11 segundos para 8 minutos e 40 segundos ± 2 minutos e 48 segundos para planos gerados utilizando o EZFluence para pacientes com câncer de mama sem envolvimento linfonodal (p-valor < 0,01) e de 23 minutos e 52 segundos ± 4 minutos e 47 segundos para planejamento manual para 15 minutos e 56 segundos ± 1 minuto e 26 segundos para planos gerados utilizando o EZFluence para pacientes com câncer de mama com envolvimento linfonodal (p-valor < 0,01). Além disso, a qualidade dosimétrica dos planos foi considerada comparável, uma vez que todos os planos manuais e automáticos foram ajustados para atender aos critérios de aceitabilidade clínica. A utilização do EZFluence demonstrou melhorar a eficiência do planejamento, mantendo a qualidade dosimétrica dos planos de tratamento.

***Palavras-chave**: planejamento automático, radioterapia, câncer de mama, automação, linfonodos*

1. Introduction

In the world, breast cancer is the most incident among women, with 2.3 million (24.5%) new cases, and the adjusted incidence rates of breast cancer are highest in both high Human Development Index (HDI) countries and those with low or medium HDI (1). According to the *Instituto Nacional do Câncer* (INCA), breast cancer represents 20.3% (74,000) of the estimated new cases of cancer in the female population in the 2023-2025 triennium in Brazil. With the exception of non-melanoma skin tumors, female breast cancer ranks as the most frequent in all Brazilian regions (2).

In the context of breast cancer, lymph node involvement is a significant concern. Sopik and Narod

noted that the likelihood of a cancer being lymph node-positive correlates with tumor size. In their investigation, among breast cancer patients with known lymph node status, 32.3% were classified as lymph node-positive at the time of diagnosis (3). Consequently, given the high incidence rates of breast cancer and the significant occurrence of lymph node involvement, a substantial number of patients are affected by this condition.

Numerous studies have elucidated the advantages of radiation therapy when combined with other modalities in the breast cancer treatment (4–6). Nonetheless, a recent investigation underscored the incapacity of Brazilian public facilities to fulfill the burgeoning demand for radiation therapy (7). Consequently, the integration of tools aimed at mitigating staff burdens, such as automated treatment planning tools, may offer invaluable assistance in this scenario. Beyond time efficiencies, these automated planning tools hold promise in consistently producing high-quality treatment plans and standardization (8,9).

Hence, the objective of this study is to evaluate the efficiency enhancements with the integration of the EZFluence tool (Radformation Inc., NY, USA) into clinical practice for the planning of radiotherapy for breast cancer with or without lymph node involvement.

2. Materials and Methods

2.1. Patient Selection

Ten patients, including five with left-sided breast cancer and five with right-sided breast cancer, were randomly selected for inclusion in the whole breast study. Additionally, eight patients with breast cancer and lymph node involvement (supraclavicular and axillary fossa) were enrolled, consisting of five with left-sided and three with right-sided cancer. This study did not require approval from an Ethics Committee, as it was conducted using data from a previously generated database with anonymized images.

Computed tomography (CT) scans were obtained while the patients were in a free-breathing state, positioned head-first and supine on a breast board, with their arms placed overhead.

2.2. Treatment protocol

The treatment protocol implemented in this study employed hypofractionation, delivering a total dose of 40.05 Gy over 15 fractions (10). Target volume delineation and organ-at-risk definition adhered to the guidelines outlined in the RTOG Breast Cancer Atlas (11). A 5 mm expansion margin from the Clinical Target Volume (CTV) was applied to establish the Planning Target Volume (PTV).

2.3. Treatment planning

The Eclipse treatment planning system (TPS) (Varian Medical Systems, Palo Alto, California), version 16, was used in conjunction with the CX treatment machine, also from Varian Medical Systems. Dose calculations were performed using version 16.1 of the Analytical Anisotropic Algorithm (AAA), while leaf motion calculations used version 16.1 of the Smart Leaf Motion Calculator (SMLC). The calculation grid was set to 2.5 mm.

According to Yoder et al.(12), the EZFluence (EZF) is designed to optimize fluence for tangent breast plans. It gathers plan information from the TPS and generates fluence intensity maps based on the patient's anatomy and plan parameters. The process starts by identifying points in the target with the goal of achieving 100% of the prescription dose. The fluence intensity maps are iteratively adjusted to balance hot spots on both sides of the breast. Finally, EZFluence ensures that the maximum dose is reduced to a specified dose goal.

The manual and EZF plans initiated with manual beam placement. For whole breast irradiation only, the physicists selected tangential fields with either single energy (6 MV) or mixed energies (6 MV and 10 MV) and used either tangent fields alone or tangent fields with an additional beam. The EZFluence plans for whole breast irradiation were created using tangent fields only with 6 MV energy. For breast plus lymph node irradiation, most of the manual and EZF plans were primarily planned with mixed energies (6 MV and 10 MV). Following beam configuration and dose calculation, the two workflows is illustrated in Figure 1. For the Field-in-Field EZF plans, the software was configured to generate a maximum of five segments per tangent beam, with each segment requiring a minimum of 5 monitor units.

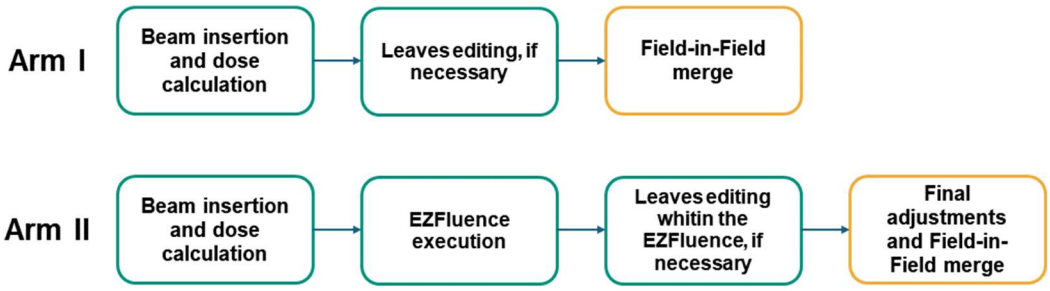

Figure 1. Study design.

2.4. Timing study

Two experienced physicists conducted manual retrospective planning for the patients and recorded the time taken to develop clinically acceptable plans, from initiation to completion. Moreover, the time required to generate plans using EZF was documented. This duration encompassed manual beam placement, dose calculation prior to EZF execution, EZF execution with leaf adjustments to meet dose constraints, plan exportation to the TPS, and final adjustments, if necessary, to fulfill the dose constraints specified by the protocol. The technique used in both manual and automated planning was the Field-in-Field method.

The computing hardware employed in this study used dual Intel(R) Xeon(R) Silver 4110 CPUs, each operating at a clock speed of 2.10 GHz.

2.5. Analysis

The compliance of the dosimetric data with the treatment protocol was assessed. Additionally, the percentage volume of the PTV that received at least 105% of the prescribed dose was evaluated. This evaluation was performed to assess the dose homogenization within the target volume.

Comparative analysis was conducted using either the t-test, Levene's test or the chi-squared test, as appropriate, with a significance level set at 0.05. Statistical analyses were performed using IBM SPSS Statistics version 21 (IBM Corporation, New York, USA).

3. Results

The planning time required by the physicists to generate the manual planning for the groups with and without lymph node involvement, as well as with the EZFluence technique distributions is shown in Figures 2 and 3.

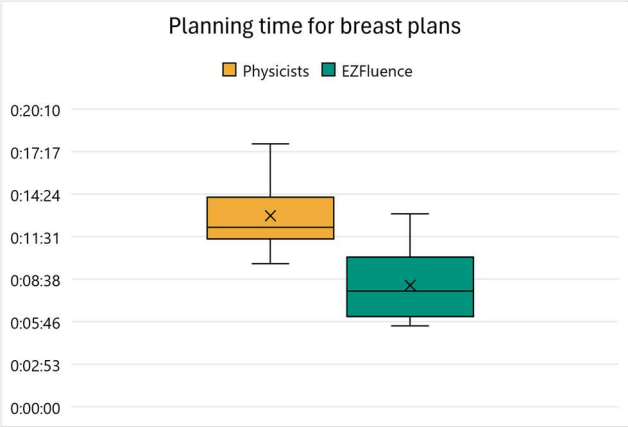

Figure 2. Planning time required to generate the manual and automatic plans for patients with breast cancer.

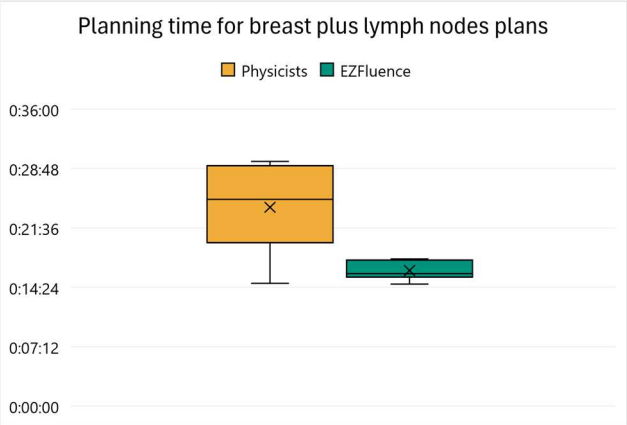

Figure 3. Planning time required to generate the manual and automatic plans for patients with breast cancer plus lymph node involvement.

The mean time required to generate plans for whole breast irradiation was 00:15:57 ± 00:04:11 for manual planning and 00:08:40 ± 00:02:48 for EZFluence planning ($p < 0.01$). For plans that included both the whole breast and lymph nodes, the mean time was 00:23:52 ± 00:04:47 for manual planning and 00:15:56 ± 00:01:26 for EZFluence planning ($p < 0.01$). The mean time differences required to generate the plans in both study arms are presented in Table 1 as absolute and relative values.

Table 1. The mean time difference required to generate the plans for both study arms is presented as absolute and relative values, represented as mean ± standard deviation.

	Breast without lymph nodes	Breast with lymph nodes
Absolute difference	00:04:38 ± 00:01:23	00:07:50 ± 00:04:19
Relative difference	36% ± 12%	30% ± 13%

Source: The author (2025).

The percentage of the PTV that received at least 105% of the dose was also collected. The results for breast cancer patients without and with lymph node involvement are shown in Figures 4 and 5. When applying the t-test, it is observed that the distributions are different among themselves, with a p-value < 0.05 for breast cancer without and with lymph node involvement.

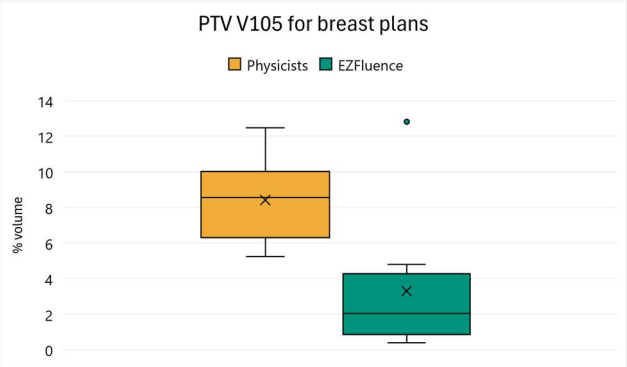

Figure 4. Percentage of the PTV that received 105% of the prescription dose for breast cancer patients.

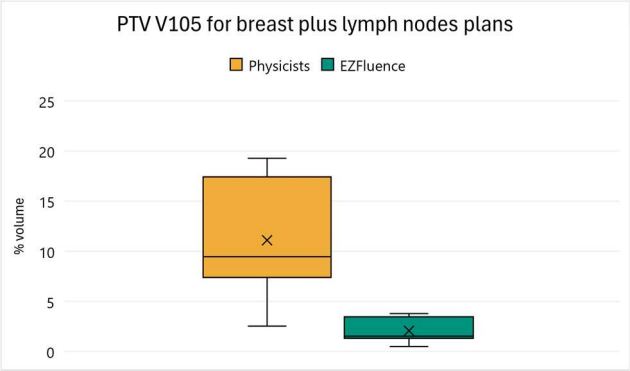

Figure 5. Percentage of the PTV that received 105% of the prescription dose for breast cancer patients with lymph node involvement.

In the comparison of V105 distributions between the EZFluence and manual plans, we observed a difference in variances for cases of breast plus lymph node irradiation (11.1±5.8 % vs. 2.1±1.2; $p < 0.050$). and for whole breast irradiation (8.4±2.3 vs 3.3±3.7; $p < 0.050$).

4. Discussion

The findings of this study highlight the effectiveness of EZFluence in producing clinically acceptable plans for breast cancer without and with lymph node irradiation. The reduction in the time required to generate these clinically acceptable plans was 36% and 30%, respectively.

It is important to note that dose constraints were not evaluated in this study due to the complexity of making a direct comparison; increased coverage might lead to a higher dose to organs at risk. Nevertheless, both the manual and EZFluence plans were designed to meet at least the acceptable dose constraints defined by the protocol, to ensure comparable planning methods. The evaluation of the percentage volume of the PTV receiving at least 105% of the prescribed dose (V105) is important, as this parameter is associated with skin toxicity (13,14). A reduction in the variance of this parameter was observed in breast plans with lymph node involvement, suggesting greater standardization in these plans. This does not imply, however, that there was no increase in the standardization of breast plans without lymph node involvement, as other dosimetric parameters were not assessed. Additionally, it was observed that V105 was significantly reduced in the EZFluence plans compared to the manual plans for both groups evaluated in this study.

As previously discussed, the elevated prevalence of breast cancer coupled with the substantial occurrence of lymph node involvement underscores the potential impact of developing automatic treatment planning tools for this treatment on the productivity of radiation therapy centers. To the best of our knowledge, this is the first work that evaluate the efficiency of the breast plus lymph node treatment planning using the EZFluence. Literature reports delineate its application solely in breast cancer irradiation, without lymph node involvement.(12,15–17).

Dragojević et al. found that EZFluence produces plans with comparable or better dosimetric quality and monitor unit efficiency than manually edited plans, highlighting EZFluence's rapid planning process and consistent plan quality (15). Similarly, Yoder et al. demonstrated that EZFluence-generated plans meet comparable dose limits for organs at risk while achieving homogeneous breast plans. The time needed to create tangential plans with EZFluence was reduced by 84.6%(12).

Some published studies have investigated automatic treatment planning for breast cancer with lymph node involvement using different tools (18,19). Marazzo et al. conducted a study using the Monaco Treatment Planning System multicriteria optimization tool to automate plans for 25 patients. The authors concluded that comparing the autoplans with clinical plans revealed similar or improved quality, resulting in a significant reduction in workload (18).

In their investigation, van Duren-Koopman et al. automated treatment plans for 15 patients employing a hybrid technique that combined two tangential and three RapidArc fields, integrating RapidPlan, in the Eclipse TPS. Their findings indicated comparable quality between the automated and manual plans, with significantly shorter planning times for the automated approach (19).

The capability to produce high-quality Field-in-Field treatment plans through EZFluence presents a significant advantage in settings where modulation technology is unavailable, a circumstance that may encompass a substantial portion of Brazilian radiation therapy centers (20). The enhancement of planning efficiency further stands out as a noteworthy benefit for resource-constrained centers.

However, a study published in 2018 evaluating medical physics practices worldwide indicated that forward-planned Field-in-Field was the most reported technique for both right and left breast radiotherapy treatments, with 75% and 70% of respondents using this method, respectively (21). Therefore, the use of Three-Dimensional Conformal Therapy is not restricted to low-resource centers and can be advantageous in improving efficiency across various scenarios.

5. Conclusions

The use of EZFluence significantly reduced the mean time required to generate treatment plans by 30 to 36% for breast cancer patients, regardless of lymph node involvement. Moreover, EZFluence plans maintained dosimetric quality comparable to manually adjusted plans, meeting clinical acceptability criteria. A notable improvement was observed in the reduction of the planning target volume receiving at least 105% of the prescription dose. These findings demonstrate that EZFluence enhances planning efficiency without compromising dosimetric quality.

Conflicts of Interest

The authors declare that they have received a complimentary software license from Radformation Inc (New York, USA) for the development of this work and GRRZ have received travel support from Radformation.

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