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# Does deep inspiration breath hold reduce plan complexity? Multicentric experience of left breast cancer radiotherapy with volumetric modulated arc therapy

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ABSTRACT

*Purpose:* Volumetric modulated arc therapy (VMAT) for left breast treatments allows heart sparing without compromising PTV coverage. However, this technique may require highly complex plans. Deep Inspiration Breath Hold (DIBH) procedure increases the heart-to-breast distance, facilitating the dose sparing of the heart. The aim of the present work was to investigate if the cardiac-sparing benefits of the DIBH technique were achieved with lower plan modulation and complexity than Free Breathing (FB) treatments.
*Methods and materials:* Ten left side breast cases were considered by two centers with different treatment planning systems (TPS) and Linacs. VMAT plans were elaborated in FB and DIBH according to the same protocol. Plan complexity was evaluated by scoring several complexity indices. A new global score index accounting for both plan quality and dosimetric parameters was defined. Pre-treatment QA was performed for all VMAT plans using EPID and Epiqa software.
*Results:* DIBH-VMAT plans were associated with significant PTV coverage improvement and mean heart dose reduction ($p < 0.003$), increasing the resulting global score index. All the evaluated complexity indices showed lower plan complexity for DIBH plans than FB ones, but only in few cases the results were statistically significant. All plans passed the gamma analysis with the selected criteria.
*Conclusions:* The DIBH technique is superior to the FB technique when the heart needs further sparing, allowing a reduction of the doses to OARs with a slightly lower degree of plan complexity and without compromising plan deliverability. These benefits were achieved regardless of the technological scenarios adopted.

## 1. Introduction

Adjuvant radiation therapy (RT) is one of essential elements of the standard care for breast cancer patients after surgery. This therapy improves local control and overall survival in patients with breast cancer [1,2]. However, with a long-term follow up, an increased incidence of cardiac events among irradiated patients has been observed [3–5]; in particular, the risk of severe cardiac events starts to increase within the first 5 years after treatment and also continues for at least 20 years [5]. The rates of major coronary events increase linearly with the mean heart dose (MHD) with a large confidence interval among authors due to different clinical endpoint chosen for the studies [6–8]. To reduce the dose to the heart and to prevent heart damage, the careful contouring of organs at risk [9,10] and the use of the latest generation of radiotherapy techniques [11] are important.

The modern technologies in RT based on inverse treatment

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planning, like intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT), could allow to achieve highly conformed dose distributions on the target volume and to spare the adjacent normal tissues and organs at risk (OAR) with respect to 3D-conformal RT, as showed in several studies for different anatomical sites [12–14].

A great debate on modern radiation therapy techniques for left breast irradiation has been also conducted in literature in the latest years. Many different techniques are available that significantly reduce radiation doses to the heart, thereby providing means to decrease cardiac toxicity risk for women undergoing such treatment [15,16]. In particular, the introduction of VMAT in clinical practice for breast region has been discussed by many groups [17–23].

The different intensity modulated techniques adopted were generally compared on the base of dosimetric parameters. IMRT/VMAT techniques have proved to ensure the heart sparing without compromising the PTV coverage [24,25].

Recently, considerable efforts have been made to further reduce the cardiac toxicity in left-sided breast irradiation by adding deep-inspiration breath-hold (DIBH) procedure to IMRT/VMAT techniques [26]. As a matter of fact, DIBH procedures increase the heart/breast distance, allowing heart dose reduction. In particular, during DIBH, the heart moves posteriorly and inferiorly due to lung expansion and diaphragmatic movements, which maximizes the distance between chest wall and heart.

Several dose planning and clinical studies have demonstrated a reduction in dose to the heart and lungs using the DIBH procedure [26]. In particular, the breath-hold technique in left-sided breast cancer 3D CRT radiotherapy with standard tangential field leads to a significant dose reduction in the heart region [27–29]. Applying an IMRT technique in breath-hold enables an additional dose reduction in these critical organs, especially in the caudal part of the radiation fields [30,31]. Moreover, higher homogeneous dose distribution can be achieved with IMRT in comparison to a 3D-CRT technique [31,32]. Regarding DIBH in combination with VMAT, Swamy et al. studied the feasibility of this procedure for locally advanced left-sided breast cancer patients and reported a significant reduction in the heart and lung dose compared to free breathing (FB) [33].

The VMAT technique allows to achieve highly conformed dose distributions on the target volume and to spare the adjacent normal tissues by the simultaneous modulation of multi-leaf collimator (MLC) movements, gantry rotation speed (GS) and dose-rate (DR) at given control points. The degree of modulation might affect the deliverability of a treatment plan due to mechanical limitations of the linac, as well as to the accuracy of dose calculations in the treatment planning system (TPS) [34] and the treatment robustness in respect to patient inter- and intra-fraction movements. Therefore, since highly modulated plans can potentially deliver unintended dose distributions to patients, various indices have been defined to assess the complexity of VMAT plans.

This study was developed to investigate if a lower plan complexity occurs when DIBH techniques are adopted instead of FB procedures in VMAT left side breast irradiation. To this aim, a multicenter comparison between FB and DIBH VMAT plans was conducted to verify whether the plan complexity is reduced with the DIBH techniques independently of the technological scenarios adopted. The comparison was based on specific plan dosimetric parameters in conjunction with complexity indices analysis. The study was completed by pre-treatment QA of all VMAT plans to assess plan deliverability.

## 2. Materials and methods

### 2.1. Patient selection and target definition

Ten patients presenting early-stage left side breast carcinoma were considered in this study. VMAT plans were elaborated on both FB and DIBH CT images by two centres equipped by different TPSs and Linac devices.

Patients were randomly selected from the internal database of patients of one RT center. Anonymized CT images, RT structures, and CT calibration files were shared with the second institution for plan optimization. Patients were placed in supine position, with both arms above the head. CT dataset was acquired with 2.5 mm thick adjacent slices. DIBH technique based on optical surface tracking technologies for CT acquisition was adopted. Prospective gating was performed in the CT room by a Sentinel™ (C-RAD AB, Uppsala, Sweden) laser scanner system and a Bright Speed CT scanner (GE Healthcare UK, Chalfont St Giles, UK): the patient's respiratory motion was monitored by the acquisition of surface data within a selected area and the CT scan was performed only when the respiratory signal is within a predetermined gating window. Visual coaching by video goggles was provided to help the patient to follow the optimal breathing pattern.

Clinical target volume (CTV) of the whole breast was the entire mammary gland. ($CTV_{breast}$). CTV for boost was the surgical bed, as defined by surgical clips placed in the lumpectomy cavity during surgery ($CTV_{boost}$). Planning target volumes ($PTV_{breast}$ and $PTV_{boost}$) were derived by adding a 5 mm margin to the CTV; PTV was limited to 5 mm within the skin surface. The main OARs considered were the heart, the ipsilateral and contralateral lungs and the contralateral breast.

### 2.2. VMAT plans and planning protocol

All FB and DIBH plans were optimized with two coplanar partial arcs of 200-220° (from target posterior entrance to the classical medial tangential one) with nominal energy of 6 MV. In the first department (DEP A), VMAT plans were studied on Elekta Monaco 5.1 TPS for an Elekta Synergy linac equipped with a multi-leaf collimator (MLCi2®) consisting of 80 paired leaves, each measuring 1 cm in width at the isocenter (ElektaAB, Stockholm Sweden). The second institution (DEP B) performed plan optimization with Varian Eclipse TPS (version 11) on a True Beam linac equipped with a Millennium MLC with 120 leaves of 5–10 mm leaf width at isocenter. A total of 40 plans were optimized.

According to a previous study [22], dose prescriptions were 40.5 Gy for the whole breast ($PTV_{breast}$) and 48 Gy for the tumor bed ($PTV_{boost}$) in 15 fractions with simultaneous integrated boost, delivering 2.7 and 3.2 Gy/fraction for the two PTVs.

Plan objectives for PTVs were: dose to the 98% of volume higher than 95% of the prescription dose for both $PTV_{breast}$ and $PTV_{boost}$ ($PTV_{breast}98\% > 38.5$ Gyand $PTV_{boost}98\% > 45.7$ Gy) and maximum dose < 107% for $PTV_{boost}$. Specific OARs constraints were: $V_{18Gy} < 5\%$ and MHD < 4 Gy for heart; $D_{mean} < 10$ Gy and $V_{20Gy} < 10\%$ for homolateral lung; $D_{mean} < 3$ Gy for contralateral lung and contralateral breast. All plan data were collected in DICOM-RT format.

### 2.3. Plan dosimetric scores

The dosimetric evaluation was based on DVH analysis of targets and organs at risk. To eliminate the bias due to different DVH calculation algorithms on different TPS, a single MIM 6.5 workstation (MIM Software Inc., Cleveland US) was used for recalculating the DVHs and specific DVH points (D98% for $PTV_{breast}$, D98% and D2% for $PTV_{boost}$, MHD and $V_{18Gy}$ for heart, $D_{mean}$ and $V_{20Gy}$ for left lung, $D_{mean}$ for right lung and breast) were collected.

### 2.4. Plan complexity scores

In this study several complexity indices that allow for a detailed analysis of the dynamic parameters involved in VMAT treatment plans were computed by using the software developed by a working group of the Catalan Society of Medical Physicists (SCFM) [35]. This software, written in MATLAB (MathWorks, Inc.), calculates complexity indices from plans in DICOM format. In particular, the following indices were evaluated:

a) total number of Monitor Units (MUs) of the plan;
b) mean MLC gap ($MLC_{gap}$), defined as the average leaf pair opening (in mm) of the leaves inside the radiation beam;
c) Leaf Travel (LT) [36] calculated in this study as the average distance (in mm) travelled by the moving leaves during the delivery of the two arcs;
d) Edge Metric (EM) [37] which computes the complexity of MLC apertures based on the ratio of MLC side edge length and aperture area. A high value of the EM score corresponds to a large difference between the positions of adjacent leaves and is closely related to the amount of tongue-and-groove effect;
e) Plan Irregularity (PI) and Plan Modulation (PM) [38] that describe the measures of the non-circularity of the MLC aperture (being 1 for a perfect circle) and the amount of multiple smaller segments, respectively;
f) Modulation Complexity Score (MCS) [39]. This metric integrates two contributions to complexity: variability in the shape of segments and variations in their area. Unlike the rest of the complexity indices, it is defined in such a way that the lower the value of the MCS the higher the complexity, being 0 and 1 the limit values;
g) total Modulation Index ($MI_{tot}$) [40] which reflects the speed and acceleration of modulating parameters such as MLC movements, dose-rate, and gantry speed.

Additionally, the maximum and minimum values of DR and GS for each DIBH and FB plan were assessed.

Furthermore, to combine the dosimetric performance of a plan and its corresponding complexity score, the following global parameter (GP) was defined as:

$$GP = (MI_{tot} \times MHD/PTV_{breast}98\%)$$

The GP was designed to take into account the target coverage, the heart sparing and the plan complexity in order to assess the overall plan quality. Both terms $MI_{tot}$ and $MHD/PTV_{breast}98\%$ were normalized to the maximum value obtained over all plans for the two techniques. This made it possible to obtain for the GP parameter a relative index (range 0–1).

The comparison of FB and DIBH dosimetric parameters and complexity indices was performed using a one-sided Wilcoxon signed ranks test for related samples (p-value $< 0.05$ was considered significant).

### 2.5. Pre-treatment QA measurements

In both clinical centers, pre-treatment verifications were carried out for all plans by using the Epiqa 5.0 software (EPIDOS sro, Bratislava), based on the GLAaS algorithm [41]: VMAT integrated images, acquired with the linac amorphous silicon portal imager, are converted into absorbed dose to water matrices at depth of maximum (1.5 cm in this case). This allows an absolute direct comparison between EPID measurements and TPS dose calculation in water phantom.

Pre-treatment quality assurance results were summarized in terms of the Gamma Agreement Index (GAI), scoring the percentage of modulated area fulfilling the gamma index criteria [42]. The gamma criteria adopted were: absolute dose global gamma analysis with dose difference (DD) and distance to agreement (DTA) respectively equal to 3%G-3 mm and 2%G-2 mm and local gamma analysis 3%L/3 mm with a lower dose threshold of 20% and a DD = 5% for dose values lower than 50% of maximum dose.

## 3. Results

### 3.1. Plan dosimetric evaluation

Both centers fulfilled target coverage requirements for all DIBH and FB plans. A significant better PTV coverage was found for DIBH treatments compared to FB ones when considering all plans for both centers ($PTV_{breast}98\%$ DIBH 39.0 ± 0.6 Gy vs FB 38.4 ± 0.6 Gy, $p < 0.035$). The FB plans did not meet the maximum dose constraint for $PTV_{boost}$ in 20% of cases, while the constraint was fulfilled for all the DIBH plans.

**Table 1**
Target coverage for DIBH and FB techniques stratified for department.

| | $PTV_{breast}98\%$ | $PTV_{boost}98\%$ | D2% $PTV_{boost}$ |
|---|---|---|---|
| DEP A | | | |
| *DIBH* | 39.4 ± 0.8 | 46.5 ± 0.5 | 49.8 ± 1.0 |
| *FB* | 38.5 ± 0.7 | 46.0 ± 1.3 | 51.5 ± 1.5 |
| *p value* | < 0.05 | – | – |
| DEP B | | | |
| *DIBH* | 38.7 ± 0.2 | 46.4 ± 0.2 | 49.0 ± 0.4 |
| *FB* | 38.3 ± 0.2 | 46.1 ± 0.2 | 49.5 ± 0.4 |
| *p value* | < 0.05 | < 0.03 | |

The comparison between target coverage in DIBH and FB techniques stratified for institutions is shown in the Table 1: plans optimized by DEP A showed higher target coverage than DEP B, without significant differences. All FB plans optimized by DEP B met the maximum dose constraint for $PTV_{boost}$. Results for target dose objective scored for each DIBH and FB plan by DEP A and B are shown in Fig. 1 in the Supplementary material.

Plan objectives regarding OARs constraints were met in all plans for DIBH technique. Dose goals for all the OARs were not achieved in FB plans: in particular regarding the heart, the MHD $< 4$ Gy requirement was not satisfied in 30% of the cases and the $V_{18Gy}$ resulted higher than requested (5% of the heart volume) in 10% of the cases. With the DIBH technique, a significant reduction in MHD and $V_{HEART18\ Gy}$ was found compared to the FB technique (MHD DIBH 2.6 ± 0.6 Gy vs FB 3.8 ± 0.8 Gy, $p < 0.003$; $V_{HEART18\ Gy}$ DIBH 0.2 ± 0.7% vs FB 1.8 ± 2.1%, $p < 0.005$), as shown in box plots in Fig. 1.

The doses to the ipsilateral lung were lower in the DIBH plans compared to FB ones, ($D_{meanLeftLung}$ DIBH 7.7 ± 0.9 Gy vs FB 8.5 ± 0.9 Gy) although differences were not statistically significant. The contralateral lung and the right breast were also slightly spared in the DIBH plans.

Results for the OARs dosimetric scores stratified for institution are reported in Table 2: all OARs dose values for DIBH plans were lower than FB plans in both departments with a statistical significance in almost all cases for DEP B.

Moreover, a significant reduction in $V_{HEART18\ Gy}$ was observed ($p < 0.01$) for FB treatments in the DEP A compared to plans from DEP B. No differences were found for MHD neither in FB nor in DIBH plans in the two institutions. Left lung mean doses were significantly lower (−12% and −15%, respectively) for DEP B plans optimized for both DIBH and FB CT studies compared to plans from DEP A. The mean dose to the Right lung was significantly reduced in DEP B DIBH plans than DEP A, while for FB optimization no difference was found between the two institutions. Regarding the right breast, $D_{mean}$ was reduced about 0.5 Gy in DEP A with respect to DEP B DIBH plans and no difference was found for FB optimization.

Results for mean dose values to the OARs scored for each DIBH and FB plan by DEP A and B are shown in Fig. 2 in the Supplementary material.

### 3.2. Plan complexity evaluation

The plan complexity was generally slightly lower for DIBH plans than for FB ones. The number of MUs, LT, EM, PM, MCS and $MI_{tot}$ indices showed a reduction in DIBH plans compared with FB optimization, while the Mean $MLC_{gap}$ and PI parameters increased their values. However, this behavior was significant only in a few cases.

The comparison between complexity indices for DIBH and FB

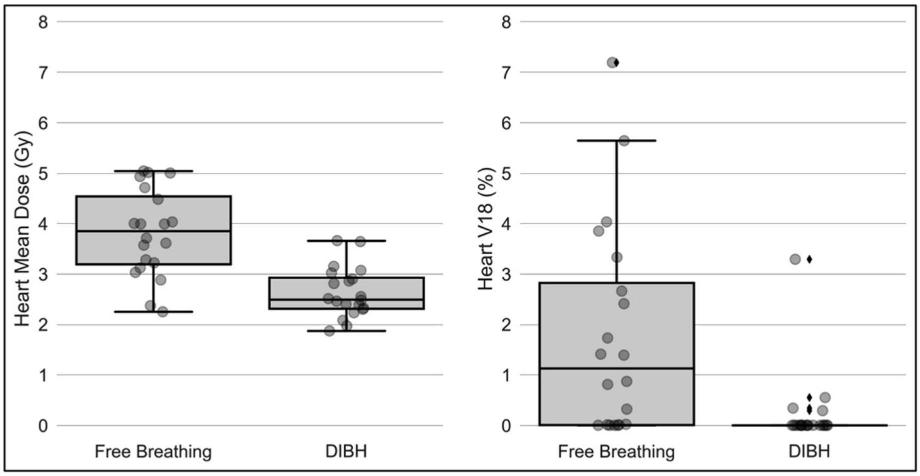


**Fig. 1.** Box plot for MHD and $V_{HEART\ 18\ Gy}$ for DIBH and FB plans.

techniques stratified for institution is shown in Table 3. The largest reduction was observed for LT, EM and MU number in DEP A treatments and in LT and $MI_{tot}$ parameters for DEP B.

The analysis of DR and GS showed a large difference between values used by DEP A and DEP B and a higher variations of these parameters occurred in DEP A plans than in DEP B.

In fact, for plan optimized in DEP A, $DR_{min}$ was equal to 47 MU/min and 48 MU/min for FB and DIBH treatments respectively, while in DEP B $DR_{min}$ was equal to 407 MU/min and 448 MU/min for FB and DIBH treatments respectively. For both FB and DIBH techniques, $DR_{max}$ was equal to 460and 600MU/min for DEP A and DEP B plans respectively.

Minimum and maximum GS ranged between 0 and 4 deg/s respectively for FB and DIBH plan optimized by DEP A and between 4 and 6 deg/s for FB and DIBH plan optimized by DEP B.

### *3.3. Global evaluation and pre-treatment verification*

The GP accounting for plan quality and dosimetric scoring resulted significant lower in DIBH plans compared to FB ones, with mean values 0.38 ± 0.09 and 0.54 ± 0.14 for DIBH and FB, respectively ($p < 0.001$). Box plots for the GP index are presented in Fig. 2.

The pre-treatment quality assurance results obtained with different dose difference and distance to agreement criteria are provided in Table 4. Both DIBH and FB optimizations yielded acceptable results with GAI (3%G-3 mm) > 95% in all cases and no statistically significant difference was found. An example of the pre-treatment quality assurance measurements analysis performed for the same patient in the two departments is shown in Fig. 3 in the Supplementary material. However, considering lower dose difference and distance to agreement criteria (i.e. 2%G-2 mm), significant differences ($p < 0.02$) were found for DEP A measurements with higher values of GAI for DIBH plans than for FB.

## 4. Discussion

This study confirmed that DIBH treatments exhibited higher target coverage and homogeneity and OARs sparing than FB, as reported by many authors [26,30–33]. In particular, relevant reduction of MHD, $V_{HEART18Gy}$ and mean lung dose with DIBH technique was demonstrated. However, FB-VMAT plans presented in general sufficient compliance with the planning protocol OAR constraints and target dose goals.

Most of published planning studies (DIBH vs FB) on breast compared PTV coverage and OAR doses sparing and delivery time and monitor unit (MU) numbers were often considered [43,44]. Conformity, homogeneity or gradient indices have also been used to compare 3D-CRT to IMRT treatment plans or even DIBH technique to FB treatments both in conformal and intensity modulated technique [45,46]. Sometimes, radiobiological parameters, such as normal tissue complication probability (NTCP), were evaluated to investigate the radiobiological implications of such dose sparing [47].

High plan complexity might be necessary in FB-VMAT plan for achieving good dosimetric results. Less complex plans offer several benefits such as more accurate dose calculations, more robust treatment delivery, better QA metrics and even lower risk associated to intra-fraction movements and patient variations. For all these reasons plans with low complexity can be considered, in general, more robust than highly complex plans. An important issue might be to evaluate the difference between FB and DIBH plans not only in dosimetric performance, but also in plan complexity.

Several complexity indices that are computed from the treatment plan parameters defined at each of the control points of the plan have been proposed in literature. Park et al. [40] introduced an overall modulation index ($MI_{tot}$) for VMAT based on the speed and acceleration analysis of modulating-parameters such as multi-leaf collimator (MLC) movements, gantry rotation and dose-rate, comprehensively.

**Table 2**
OARs dosimetric results for DIBH and FB techniques stratified for department.

| | Dmean Heart | $V_{18Gy}$ Heart | Dmean Left Lung | $V_{20Gy}$ Left Lung | Dmean Right Lung | Dmean Right Breast |
|---|---|---|---|---|---|---|
| DEP A | | | | | | |
| *DIBH* | 2.6 ± 0.5 | 0.0 ± 0.1 | 8.2 ± 0.6 | 8.0 ± 0.8 | 2.2 ± 0.5 | 1.6 ± 0.8 |
| *FB* | 3.8 ± 0.8 | 0.5 ± 1.3 | 8.8 ± 0.8 | 8.1 ± 1.9 | 2.3 ± 0.6 | 2.0 ± 0.9 |
| *p value* | < 0.01 | – | – | – | – | – |
| DEP B | | | | | | |
| *DIBH* | 2.6 ± 0.6 | 0.4 ± 1.0 | 7.2 ± 0.8 | 8.0 ± 1.5 | 1.5 ± 0.3 | 2.0 ± 0.5 |
| *FB* | 3.8 ± 0.7 | 3.0 ± 2.0 | 7.9 ± 0.7 | 9.5 ± 1.5 | 2.1 ± 0.5 | 2.1 ± 0.4 |
| *p value* | < 0.01 | < 0.005 | < 0.04 | < 0.02 | < 0.04 | – |

**Table 3**
Mean values and standard deviations of complexity indices calculated for the DIBH and FB plans in DEP A and DEP B, respectively. Percent differences between DIBH and FB results and p value are also reported.

| | MU | Mean $MLC_{gap}$ (mm) | LT (mm) | ($mm^{-1}$) | PI | PM | MCS | $MI_{tot}$ |
|---|---|---|---|---|---|---|---|---|
| DEP A | | | | | | | | |
| *DIBH* | 920 ± 81 | 36.2 ± 2.2 | 1615 ± 113 | 0.10 ± 0.01 | 5.6 ± 0.6 | 0.86 ± 0.01 | 0.29 ± 0.01 | 1.31 ± 0.04 |
| *FB* | 985 ± 124 | 34.1 ± 2.9 | 1785 ± 153 | 0.12 ± 0.01 | 5.3 ± 0.6 | 0.87 ± 0.01 | 0.29 ± 0.02 | 1.33 ± 0.05 |
| *% Diff.* | −7.1% | 5.8% | −10.5% | −18.6% | 5.4% | −1.2% | – | −1.5% |
| *p value* | – | < 0.02 | < 0.05 | < 0.05 | – | – | – | – |
| DEP B | | | | | | | | |
| *DIBH* | 893 ± 69 | 21.9 ± 5.1 | 817 ± 33 | 0.27 ± 0.02 | 17.8 ± 0.9 | 0.82 ± 0.01 | 0.17 ± 0.02 | 0.94 ± 0.04 |
| *FB* | 909 ± 94 | 21.7 ± 5.2 | 882 ± 49 | 0.28 ± 0.03 | 17.4 ± 1.8 | 0.83 ± 0.02 | 0.17 ± 0.03 | 0.98 ± 0.05 |
| *% Diff.* | −1.8% | 0.9% | −8.0% | −3.7% | 2.2% | −1.2% | – | −4.3% |
| *p value* | – | – | < 0.02 | – | | – | – | – |

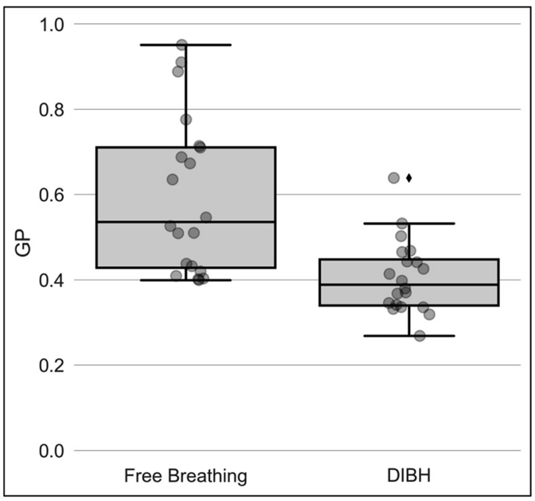


**Fig. 2.** Box plot for GP = ($MI_{tot}$x$MHD/PTV_{breast}$98%) evaluated for all DIBH and FB plans.

**Table 4**
Gamma agreement index passing rates (%) for DIBH and FB techniques in both institutions. Data are presented as the mean values and standard deviations; p value is also shown.

| | GAI (%) (3%G, 3 mm) | GAI (%) (2%G, 2 mm) | GAI (%) (3%L, 3 mm) |
|---|---|---|---|
| DEP A | | | |
| *DIBH* | 97.7 ± 0.8 | 88.0 ± 2.0 | 87.8 ± 3.0 |
| *FB* | 97.2 ± 0.7 | 85.4 ± 2.4 | 87.4 ± 4.0 |
| *p value* | – | < 0.02 | – |
| DEP B | | | |
| *DIBH* | 99.8 ± 0.2 | 97.7 ± 1.1 | 98.6 ± 1.0 |
| *FB* | 99.8 ± 0.2 | 97.7 ± 0.9 | 98.8 ± 0.9 |
| *p value* | – | – | – |

Hernandez et al. [48] showed that treatment plans with similar dose distributions may differ greatly in their complexity and that several complexity metrics should be evaluated because no single metric is sufficient for all TPSs. Nevertheless, plan complexity metrics have never been evaluated, to our best knowledge, for VMAT breast treatments. These complexity indices allow for a detailed analysis of the dynamic parameters involved in treatment plans, which makes them more appropriate for VMAT than 'fluence-based' indices [48].

In this study many complexity metrics were investigated and the results showed that the plan complexity was generally lower for DIBH than for FB, even if this behavior was statistically significant only in few cases.

The analysis of complexity indices revealed remarkable differences in the optimization engines and sequencers for the two departments involved in this work, which prioritized the modulation of different plan parameters. Some discrepancies appeared between complexity metrics such as LT, EM, PI and $MI_{tot}$ for DEP A and B both for DIBH and FB plans. The indices LT, EM and PI focus on the assessment of movements and shapes of MLCs and are higher for plans optimized by the Eclipse TPS, which tends to use smaller and more complex MLC apertures. On the other hand, $MI_{tot}$ was increased in plans that further modulate the DR and the GS, as occurred in plans generated with the Monaco TPS. These discrepancies can be explained by the large differences in the modulation of dynamic parameters used by the TPS to achieve the dosimetric goals. This result is coherent with literature, where a large spread in some of the complexity indices was observed depending on the TPS [48]. Moreover, the variability of complexity metrics depended on the TPS, which indicates that the ability of each index to discriminate between plans depends on the TPS.

Therefore, the comparison between the two planning techniques can benefit from assigning to each plan a single overall plan quality score that incorporates multiple plan complexity and dosimetric metrics [49,50]: the use of a scoring index of plan quality has been applied in multiple contexts, but it has never been adopted up to now for the comparison between FB and DIBH VMAT breast plans. In this study a global parameter GP, accounting for plan quality and dosimetric scoring, was defined to assess the overall plan quality. GP was not intended to provide a universal plan quality score for breast planning, but was simply a tool for evaluating plan variability between techniques [51]. The evaluation of GP showed a significant difference between DIBH and FB plans optimized in the two enrolled institutions: GP resulted lower for DIBH than FB procedures due to the fact that DIBH plans had definitely better dosimetric characteristics and a slightly lower plan complexity with respect to FB plans.

Moreover, our results indicated that DIBH offered a better overall plan quality than FB plans regardless of the technological scenarios adopted. This indicates that the TPSs used the benefit associated to the DIBH technique to improve the dosimetric plan performance while keeping a similar level of plan complexity. In other words, even if DIBH plans might be considerably less complex because in principle the optimisation engine could fulfill more simply the dose goals, the DIBH plans produced have a slightly lower complexity than FB ones and all the additional benefits were used to improve the dosimetric distribution.

Many investigators have reported that plan complexity indices are correlated with QA metrics [36–40]. Masi et al. [36] found a significant correlation between gamma index passing rates obtained by pre-treatment dosimetric verification of VMAT plans and both LT and MCS. Nicolini et al. [34] found that the agreement between planned and delivered doses decreased as complexity increased. In the present study all plans verifications produced satisfactory QA results and the fact that QA metrics were similar is compatible with the fact that DIBH plans were only slightly lower complex than FB plans.

Despite the overall good agreement for dose profiles in pre-treatment QA verifications, the difference in the gamma pass rates between the two institutions could be attributed to the impact of a threshold analysis on such different type of fluences: for DEP A the irradiated volumes are larger, encompassing more low-inter medium dose levels and relatively flat profiles sub-regions, thus including different area of interest and scoring lower gamma pass rates.

Thus, the evaluation of the differences between FB and DIBH VMAT plans not only in dosimetric performance, but also in plan complexity and deliverability, carried out in this study showed that the DIBH technique is clearly better when the heart needs further sparing, because it allows a further reduction of the OAR doses with a slightly lower level of plan complexity and without compromising plan deliverability.

## 5. Conclusions

For left breast cancer patients treated with VMAT, DIBH procedures offer a better overall plan quality than FB plans. VMAT-DIBH plan allows to significantly reduce OARs doses, reducing plan complexity and without compromising plan deliverability. This means that the additional benefits provided by the DIBH technique are used by the TPSs mostly to further improve the dosimetric plan performance and only slightly to reduce the level of plan complexity. Moreover, this study shows that the superiority of DIBH treatments is achieved regardless of the technological scenarios adopted.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejmp.2019.02.018.

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