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Original paper

Is the lack of respiratory gating prejudicial for left breast TomoDirect treatments?

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ABSTRACT

Background and purpose: TomoDirect (TD) can only operate in free-breathing. The purpose of this study is to compare TD with breath-hold 3D conformal radiotherapy (3DCRT) and intensity modulated radiotherapy (IMRT) techniques for left breast treatments, and to determine if the lack of respiratory gating is a handicap for cardiac sparing.

Materials and methods: 15 patients treated for left breast had two computed tomography simulation, in free breathing (FB) and in deep-inspiration breath-hold (DIBH). Four treatments were planned: TD-FB, 3DCRT-FB, 3DCRT-DIBH and IMRT-DIBH. Dose to PTV, heart, lungs, right breast and patient were compared.

Results: A slightly lower cardiac mean dose is found for 3DCRT-DIBH than for TD-FB group (1.99 Gy Vs 2.89 Gy, $p = 0.0462$), while no statistical difference is found for heart V_{20}. TD-FB plans show the best PTV dose homogeneity (0.053, $p < 0.001$) and the lowest left lung mean dose (5.16 Gy, $p < 0.001$). No major differences are found for the other organs.

Conclusions: TomoDirect and breath-hold 3DCRT are complementary techniques for left breast treatments: for a minority of patients, respiratory gating is mandatory to lower cardiac dose; for the remaining majority of patients, TomoDirect achieves better PTV homogeneity and reduced left lung dose, with cardiac dose equivalent to 3DCRT-DIBH.

Introduction

Breast cancer is the most common women cancer, with an incidence rate of over one million cases per year worldwide [1]. Radiation therapy has a major role in the management of this disease, to reduce local recurrence and improve overall survival probability [2]. This treatment modality has long been suspected of causing cardiac toxicities, especially for left breast cases. These toxicities were confirmed notably by a large follow-up work conducted by Darby et al. over 2158 patients [3], which showed that the risk of coronary events would increase by 7.4% per gray delivered to the heart, even if the possibility of a threshold could not be excluded. The beneficial role of radiotherapy is indisputable in breast cancer treatments, and new radiation techniques have been introduced to reduce the irradiated heart volume.

One possibility to reduce this volume is to use breath-hold methods. Several devices, widely described in the literature [4,5], have the objective of delivering treatment when the heart is the most distant from the chest wall [6]: in a recent literature review including studies published by 18 teams, Drew Latty et al. showed that deep-inspiration breath-hold (DIBH) provides a relative reduction in mean heart dose ranging from 26.2% to 75% [7].

Another way to reduce the cardiac dose is intensity modulated radiotherapy (IMRT) by conventional linac or TomoDirect. Whatever the IMRT technique used on a conventional linac (forward-planned, reverse planned, hybrid-IMRT ...), dosimetric comparison to a 3D conformal radiotherapy (3DCRT) generally shows a better homogeneity in the target volume and a decrease in the mean dose to the heart [8]. The TomoDirect technique (Accuray, USA), which is a treatment modality of Tomotherapy by fixed angle [9], was also investigated in various comparisons with 3DCRT and static IMRT [8–10]. Dosimetric results for PTV coverage are in favor of TomoDirect [10]. For heart and lung ipsilateral, the average doses obtained by TomoDirect are reduced compared to those obtained by 3DCRT [8,9,11].

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Other studies have shown that combining the respiratory gating with static IMRT would further reduce the average dose to the heart: by comparing IMRT and 3DCRT delivered both with respiratory gating, Mast has shown that IMRT can reduce the average cardiac dose by 17% [12].

TomoDirect is not compatible with respiratory gating techniques, mainly because an unpredictable time delay (from several second to >10 s) occurs between the launch of the tomotherapy treatment beam by the operator and the effective beam delivery. This lack of respiratory gating can potentially be a handicap for reducing dose to the heart. To check if the modulation level of the TomoTherapy allows overcoming this handicap, we have compared the dosimetric performance of left breast TomoDirect treatments, which can be only performed in free breathing, with those by static IMRT and 3DCRT associated with DIBH.

Materials and methods

Patient selection and image acquisition

15 patients previously treated at Paul Strauss Cancer Center by 3DCRT with DIBH for left breast alone without nodes were enrolled in this study. The average age is 55 years, and the average volume of the PTV = 726 cm^3. Detailed characteristics for the 15 patients are given in Appendix 1.

All patients treated for left breast in our hospital have two computed tomography (CT) simulation: one in free breathing (FB) and another one in DIBH, the same day and in the same position. The radiotherapist checks visually (no quantitative criteria) on CT slices if DIBH may potentially help to increase the ribs to heart distance, and then chooses to plan treatment with or without DIBH. It is important to note that the 15 patients recruited for this study are therefore a priori patients for whom the DIBH reduces cardiac doses.

The CT simulation is performed with the patient in supine position and arms above the head using a Posiboard (CIVCO, USA). 2.5 mm CT axial images are obtained at 120 kV using a GE Optima 580 RT CT (General Electric, USA).

Note that using fast helical CT for planning of patients with significant breast motion due to breathing may not properly account for motion effect when treating in FB, resulting in differences between planned and delivered doses. Untagged average 4DCT data are therefore recommended for planning in FB cases [13].

DIBH method

The breath-hold system used is SDX (SDX, Dyn'R, France), a spirometer dedicated to the practice of breath-hold [4]. Respiratory gating is performed in inspiration by voluntary breath-hold, during both image acquisition and irradiation. The patient is able to monitor its breathing curve with video glasses (Fig. 1).

The reference level is defined as 75 to 85% of the maximal inspiratory capacity, depending on the patient compliance: if possible, a 85% level is preferred, to maximize the potential cardiac sparing. Three consecutive acquisitions of 20–25 s are then performed, to ensure the patient could comfortably maintain the breathing level.

Delineation and dose constraints

The left and right lung, right breast and heart are delineated with Focal v.4.80.01 (Elekta, Sweden) on both FB and DIBH scans. The PTV is created with an isotropic extension of 5 mm around the left breast, and a 5 mm skin retraction. To control the dose in healthy areas excluding organs at risk (OARs) for IMRT planning,

Fig. 1. Patient positioning during computed tomography simulation, with the SDX spirometer (SDX, Dyn'R, France). An acquisition is also made in free breathing without the SDX system, with identical equipment and positioning.

two optimization structures are created: PTV + 1 mm and PTV + 5 cm. PTV + 1 mm is only used for overlapping, to avoid any pixel overlap between PTV and OARs. PTV + 5 mm is used to fasten dose gradient around the PTV and to avoid hot spots in healthy region not covered by OARs. An example of delineation is given in Fig. 2.

The prescription dose is 50 Gy in 25 fractions of 2 Gy. As part of this dosimetric study, the additional boost to the tumor bed is not planned. PTV constraints are $D_{98\%} > 95\%$ (47.5 Gy) and $D_{2\%} < 107\%$ of the prescribed dose (53.5 Gy). Regarding the OARs, the objective is to minimize the delivered doses while trying to respect PTV constraints.

Treatment planning

3DCRT treatments are planned using XiO Version 4.80 (Elekta, Sweden) for both the FB (3D-FB) and the DIBH CT scans (3D-DIBH). Plans consist of opposed tangential fields (2 or more) that use 6 MV and 15 MV photon beams. Dynamic wedge filters, MLC, different beam weighting and point prescription may be use to optimize dose distribution.

TomoDirect planning is performed using Tomotherapy HD planning station version 5.0.1.7 (Accuray, USA), only on the FB CT

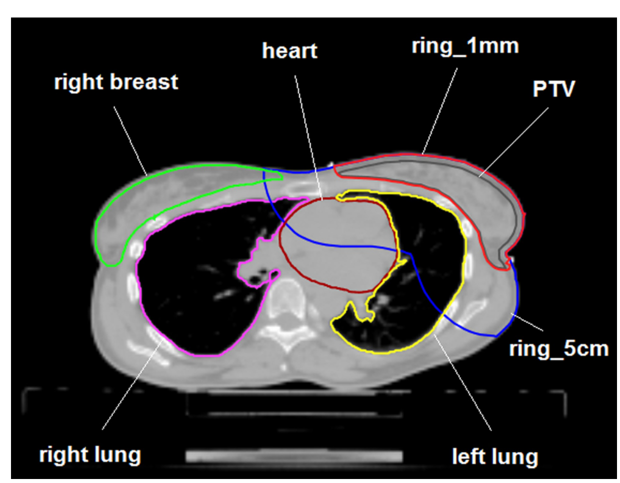

Fig. 2. Example of delineation on a deep inspiration breath-hold Computed Tomography simulation scan; ring_1 mm and ring_5 cm are helping structures for IMRT optimization.

scan (TD-FB). The prescribed dose is 50% of the PTV. Two tangential beams are created with the same angulations than for 3DCRT, with two additional beams at ±5°, making sure to not irradiate directly the right breast. A field width of 5 cm, a pitch of 0.5 cm and a modulation factor set to 2 are used. Treatment is performed in IMRT mode with three "flash" leaves left open. The dose calculation grid "normal" is used for optimization ($4.10 \times 4.10\ mm^2$) and "fine" when calculating the final dose ($2.05 \times 2.05\ mm^2$). Dynamic Jaw option is not enabled.

Static IMRT planning is performed using Eclipse Version 11.0.47 using the DVO.11.0.31 optimization algorithm (Varian Medical Systems, USA) in sliding window mode, only on the DIBH CT scan (IMRT-DIBH). Two tangential beams are created with the same angulations than for 3DCRT, also with two or more additional beams at ±5°.

Plan review

The 60 treatment plans corresponding to the 15 patients calculated in TD-FB, 3D-FB, 3D-DIBH and IMRT-DIBH are exported to ARTIVIEW (Aquilab, France), where 10 dosimetric parameters are evaluated for each plan. Fig. 3 shows a representative isodose distribution for the 4 plans. $D_{2\%}$ (near-max), $D_{98\%}$ (near-min) and homogeneity index (HI) are used to quantify the quality of PTV coverage: $HI = (D_{2\%} - D_{98\%})/D_{50\%}$ [14]. For OARs, we record the average dose to the heart, to the left and right lungs, the volume of the heart and left lung receiving at least 20 Gy (V_{20}), and the maximum dose to the right breast. We also calculate the patient integral dose (ID), with ID = average dose to patient ∗ patient volume [15].

Statistical analysis

For each variable, data are composed of repeated measurements among 15 patients. To deal with pseudo-replication among these repeated measurements, linear mixed effects models were fitted with identity of the patient as random effect and technique, breast volume and its interaction as fixed effects. A backward model selection was performed on the base of the lowest Akaike information criterion (AIC). Data were log-transformed when needed to assess normality of the residuals. Pairwise comparisons tests were performed with a Tukey correction.

Significance level of statistical tests was set to 5%. Statistical analysis was performed with R [16] and its packages nlme and multcomp.

Results

The detailed dosimetric results of the 60 treatment plans are given in Appendix 2. The AIC and best model statistical analysis results are given in Appendix 3. A statistical effect was found between treatment modality and all dosimetric parameters, except for the right breast ($p = 0.738$).

The mean dosimetric group values and p-values for pairwise comparison between modalities are summarized in Table 1: for example, PTV HI is significantly lower for TD-FB (HI = 0.053) compared to other techniques (HI = 0.113 to 0.117, with $p < 0.001$ for TD-FB Vs all modalities).

For each model except the one explaining the integral dose, model selection led to an optimal model with only the technique as fixed effect. However, the effect of breast volume remains very low even for integral dose. So, as observed by Michalski [10], we found that neither interaction between breast volume and technique nor breast volume have an effect on dosimetric parameters, including PTV homogeneity.

Discussion

Heart

The most irradiating technique for the heart is by far 3DCRT in free breathing: the mean cardiac dose is equal to 4.94 Gy in 3D-FB, while it is less than 3 Gy for the 3 other techniques.

TomoDirect gives higher dose to the heart than 3D-DIBH, with a 31% increase for the mean cardiac dose, however at significance level limit ($p = 0.0462$). The average gain for the mean dose to

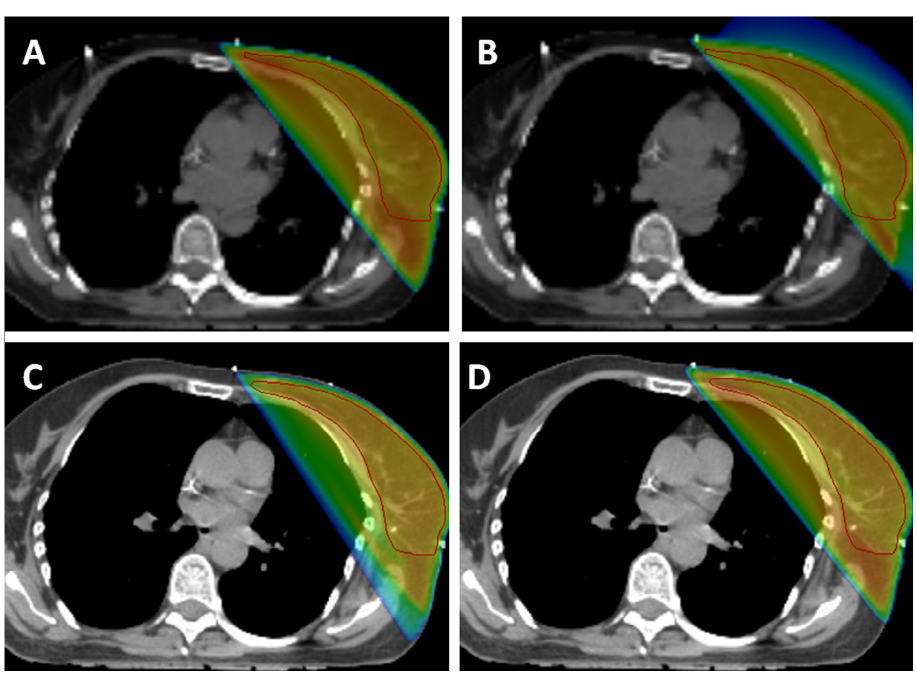

Fig. 3. An example of isodose distribution for (A) 3D-FB, (B) TD-FB, (C) IMRT-DIBH and (D) 3D-DIBH plans (patient 7). The isodose represents a dose >20 Gy.

Table 1
Average results for the 15 patients to the PTV and OARs for TD-FB, 3D-FB, 3D-DIBH and IMRT DIBH planning techniques, including the *p*-values for pairwise comparisons (grayed cell when significant effect is observed).

	mean ± SD				*p*-Value					
	TD-FB	3D-FB	3D-DIBH	IMRT-DIBH	TD-FB *vs* 3D-FB	TD-FB *vs* 3D-DIBH	TD-FB *vs* IMRT-DIBH	3D-FB *vs* 3D-DIBH	3D-FB *vs* IMRT-DIBH	3D-DIBH *vs* IMRT-DIBH
PTV										
$D_{2\%}$ (Gy)	51.05 ± 0.31	52.91 ± 0.66	52.97 ± 0.41	52.58 ± 0.78	<0.001	<0.001	<0.001	0.985	0.221	0.105
$D_{98\%}$ (Gy)	48.42 ± 0.52	47.25 ± 0.66	47.13 ± 0.75	46.86 ± 1.62	<0.001	<0.001	<0.001	0.975	0.567	0.817
HI	0.053 ± 0.013	0.113 ± 0.018	0.117 ± 0.020	0.114 ± 0.038	<0.001	<0.001	<0.001	0.946	0.998	0.982
Heart										
D_{mean} (Gy)	2.89 ± 1.38	4.94 ± 2.44	1.99 ± 1.38	2.36 ± 1.48	<0.001	0.0462	0.415	<0.001	<0.001	0.713
V_{20Gy} (%)	3.72 ± 2.98	8.16 ± 4.99	2.2 ± 2.38	2.35 ± 2.83	<0.001	0.156	0.237	<0.001	<0.001	0.997
Left Lung										
D_{mean}(Gy)	5.16 ± 2.20	7.89 ± 3.15	6.81 ± 2.31	7.60 ± 2.25	<0.001	<0.001	<0.001	0.007	0.822	0.090
V_{20Gy} (%)	9.13 ± 5.03	14.98 ± 6.55	12.73 ± 4.81	14.36 ± 5.32	<0.001	<0.001	<0.001	0.015	0.848	0.134
Right Lung										
D_{mean} (Gy)	0.25 ± 0.06	0.18 ± 0.06	0.16 ± 0.05	0.12 ± 0.07	<0.001	<0.001	<0.001	0.114	<0.001	<0.001
Right Breast										
D_{max} (Gy)	1.80 ± 0.40	2.79 ± 3.62	1.74 ± 0.9	2.09 ± 0.92	0.979	0.891	0.999	0.683	0.953	0.937
Patient										
ID ($Gy.cm^3$)	106.4 ± 39.1	105.0 ± 34.1	98.85 ± 34.72	100.8 ± 34.20	0.876	<0.001	0.013	0.005	0.100	0.730

Abbreviations: SD: standard deviation. ID: integral dose. HI: homogeneity index. $D_{2\%}$, $D_{98\%}$: dose encompassing 2% and 98% of the volume respectively. V_{20Gy} (%): volume receiving 20 Gy. TD-FB: TomoDirect in free-breathing. 3D-FB: 3D conformal radiotherapy in free-breathing. 3D-DIBH: 3D conformal radiotherapy in deep inspiration breath-hold. IMRT-DIBH: intensity modulated radiotherapy in deep inspiration breath-hold.

the heart associated with the respiratory gating relative to TomoDirect is 0.9 Gy, which remains relatively small in terms of absolute dose. There is no significant difference for the heart V_{20} between these two techniques ($p = 0.156$). Note that these results may be different with a higher DIBH level, potentially resulting in better cardiac sparing with the 3D-DIBH technique.

If we look at TomoDirect and 3D-DIBH plans per patient (see Fig. 4) and we choose 3 Gy as a limit not to exceed, only 3 of 15 patients benefit from respiratory gating. Remind that we have included only patients who should benefit from respiratory gating (cf. Section 2). With a randomized selection, the number of patients for whom TomoDirect and 3D-DIBH would be equivalent for cardiac sparing should theoretically be even more important.

Without respiratory gating, the heart is better saved with TomoDirect: mean dose to the heart is reduced by 41% relative to the 3D-FB ($p < 0.001$), which is consistent with the results obtained by Chi (52%) [17] and Michalski (28%) [10].

When comparing 3DCRT with and without respiratory gating, we find that DIBH helps reducing the average dose and V_{20} to the heart respectively by 60% and 73% ($p < 0.001$). These results are comparable to those of the review of Latty who showed that respiratory gating achieves an average reduction of 51% in cardiac mean dose [7].

We did not observe any significant difference for heart sparing between 3DCRT and IMRT both with breath-hold (D_{mean} $p = 0.713$; V_{20} $p = 0.997$). These results are contrary to those of Mast, which shows a slight gain of 17% on cardiac mean dose when IMRT is combined with DIBH [12]. The differences between algorithms and planning techniques used may explain the conflict between our results and those of literature.

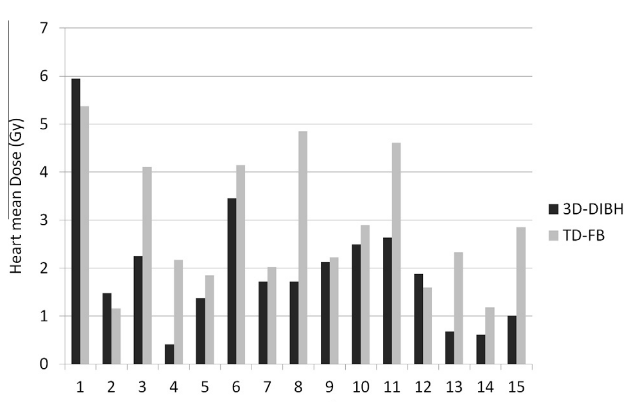

Fig. 4. Mean dose to the heart for deep inspiration breath-hold 3D conformal radiotherapy (3D-DIBH) and free-breathing TomoDirect (FB-TD) per patient.

PTV coverage

PTV $D_{2\%}$ and $D_{98\%}$ are statistically better for TD-FB than for the other techniques studied. PTV near-min dose is significantly better for TomoDirect ($D_{98\%} = 48.4$ Gy) than for 3DCRT or IMRT

Appendix 1
Characteristics of the 15 patients enrolled in this study.

Patient #	Age	PTV volume (cm^3)
1	51	795
2	66	518
3	40	317
4	64	378
5	66	411
6	38	1729
7	45	430
8	42	331
9	53	778
10	58	826
11	55	289
12	54	1117
13	60	713
14	72	1177
15	68	1082
Mean	55	726
SD	11	412

Abbreviations: SD: standard deviation.

Appendix 2
Detailed results for each patient.

Patient #	Breast Vol. (cm^3)	Technique	PTV			Heart		Left lung		Right lung	Right breast	Patient
			D_2 (Gy)	D_{98} (Gy)	IH	D_{mean} (Gy)	V_{20} (%)	D_{mean} (Gy)	V_{20} (%)	D_{mean} (Gy)	D_{max} (Gy)	ID (Gy cm^3)
1	795	3D-DIBH	52.7	46.5	0.124	5.95	8.92	10.66	20.4	0.27	2.08	117.1
		3D-FB	52.6	46.5	0.122	9.06	15.72	11.44	22.0	0.35	2.69	124.0
		IMRT-DIBH	51.7	46.8	0.098	6.09	9.37	10.94	22.5	0.30	2.09	117.5
		TD-FB	50.8	48.4	0.048	5.37	8.18	6.47	11.6	0.39	1.85	121.0
2	518	3D-DIBH	53.2	47.4	0.116	1.48	0.63	9.37	17.5	0.16	2.76	88.3
		3D-FB	53.9	47.4	0.131	3.00	3.25	12.25	23.4	0.21	2.79	92.1
		IMRT-DIBH	52.2	48.3	0.077	1.28	0.39	9.76	19.3	0.10	2.03	85.6
		TD-FB	51.1	48.7	0.048	1.16	0.44	8.04	15.5	0.23	1.22	83.1
3	317	3D-DIBH	53.2	47.7	0.111	2.25	1.99	6.03	10.7	0.15	2.69	69.5
		3D-FB	53.2	46.8	0.128	6.47	10.60	5.50	9.7	0.17	3.29	72.2
		IMRT-DIBH	53.6	48.6	0.099	2.02	1.30	7.99	15.7	0.14	2.10	71.8
		TD-FB	50.9	48.2	0.055	4.11	6.72	3.08	4.7	0.22	1.37	66.9
4	378	3D-DIBH	53.1	47.0	0.122	0.41	0.00	3.98	7.3	0.08	1.31	66.6
		3D-FB	52.9	46.9	0.120	2.45	3.86	5.07	9.6	0.07	2.03	66.9
		IMRT-DIBH	52.4	47.8	0.092	0.79	0.00	4.62	7.6	0.07	2.32	72.0
		TD-FB	51.6	48.4	0.062	2.17	2.08	4.00	6.5	0.16	2.21	79.7
5	411	3D-DIBH	52.8	46.9	0.119	1.37	1.33	5.18	9.6	0.15	1.42	53.1
		3D-FB	53.0	47.6	0.109	5.56	9.71	5.67	10.5	0.16	0.69	78.7
		IMRT-DIBH	52.7	47.7	0.099	1.50	0.56	5.48	9.4	0.05	1.84	70.7
		TD-FB	50.8	48.8	0.039	1.85	1.33	1.84	1.5	0.20	1.36	69.3
6	1729	3D-DIBH	53.2	45.7	0.152	3.46	5.03	8.57	16.3	0.19	1.74	170.7
		3D-FB	52.9	46.4	0.130	7.61	13.41	9.69	18.5	0.21	1.80	181.0
		IMRT-DIBH	53.0	45.4	0.151	4.77	7.36	10.32	21.5	0.19	2.14	178.9
		TD-FB	51.3	47.8	0.070	4.15	5.48	6.43	11.4	0.35	2.28	191.4
7	430	3D-DIBH	51.9	47.5	0.087	1.72	1.24	7.06	13.1	0.10	3.03	83.3
		3D-FB	51.0	47.0	0.080	4.33	6.41	9.75	18.7	0.16	3.54	92.6
		IMRT-DIBH	52.0	47.6	0.090	0.91	0.00	7.29	14.2	0.07	1.94	79.3
		TD-FB	51.0	47.9	0.063	2.02	2.28	6.64	12.7	0.21	1.45	85.4
8	331	3D-DIBH	53.2	47.7	0.110	1.72	2.11	7.52	14.6	0.16	1.00	66.3
		3D-FB	53.0	47.8	0.104	6.52	12.00	9.74	19.3	0.19	1.27	67.9
		IMRT-DIBH	51.7	47.6	0.082	1.92	1.40	7.45	13.6	0.11	1.95	63.9
		TD-FB	50.7	48.8	0.038	4.85	8.87	6.86	12.6	0.22	2.17	69.1
9	778	3D-DIBH	53.0	48.0	0.101	2.13	2.54	8.04	15.9	0.20	1.39	114.7
		3D-FB	52.9	47.8	0.102	2.44	3.35	7.74	15.2	0.18	1.26	111.1
		IMRT-DIBH	52.4	47.5	0.098	2.26	1.13	8.18	15.4	0.16	3.85	109.9
		TD-FB	50.9	48.5	0.048	2.22	2.19	7.17	14.5	0.32	1.89	124.7
10	826	3D-DIBH	52.3	48.3	0.080	2.49	2.48	3.21	4.8	0.13	3.38	104.8
		3D-FB	52.2	48.6	0.071	4.58	6.52	2.25	2.9	0.12	3.31	110.0
		IMRT-DIBH	51.3	46.2	0.102	2.87	3.42	4.33	7.0	0.08	2.74	103.9
		TD-FB	51.2	49.1	0.041	2.90	3.66	1.72	1.4	0.21	1.96	114.4
11	289	3D-DIBH	53.3	47.2	0.122	2.63	4.25	7.41	14.2	0.12	0.79	56.1
		3D-FB	53.4	47.3	0.122	8.94	17.28	9.83	19.3	0.16	0.92	64.9
		IMRT-DIBH	52.1	47.6	0.090	2.95	4.38	8.75	16.3	0.05	3.07	59.5
		TD-FB	50.9	48.0	0.059	4.61	7.98	5.76	10.8	0.16	1.56	56.7
12	1117	3D-DIBH	53.2	46.8	0.129	1.88	1.97	8.44	16.2	0.23	2.12	125.8
		3D-FB	53.4	46.9	0.129	2.75	3.67	7.99	15.3	0.24	15.35	128.8
		IMRT-DIBH	53.7	46.6	0.142	2.47	2.34	8.98	18.0	0.17	2.67	125.5
		TD-FB	50.9	48.1	0.055	1.59	0.98	5.96	11.1	0.26	2.22	126.8
13	713	3D-DIBH	52.9	47.8	0.102	0.68	0.00	6.05	11.2	0.14	0.65	91.5
		3D-FB	53.3	48.2	0.101	3.91	6.39	7.61	14.5	0.15	1.00	99.0
		IMRT-DIBH	53.5	47.9	0.113	1.09	0.00	6.80	11.8	0.11	2.16	94.8
		TD-FB	50.8	49.3	0.030	2.33	2.07	4.43	7.5	0.26	2.27	101.9
14	1177	3D-DIBH	53.3	46.8	0.131	0.61	0.00	2.47	3.5	0.12	0.97	143.5
		3D-FB	53.3	47.3	0.121	1.05	0.41	2.39	3.3	0.11	0.94	147.8
		IMRT-DIBH	52.8	42.2	0.212	1.21	0.28	3.63	5.0	0.06	0.27	140.6
		TD-FB	51.7	48.9	0.056	1.18	0.00	1.62	0.8	0.24	1.18	166.3
15	1082	3D-DIBH	53.3	45.9	0.149	1.01	0.46	8.10	15.7	0.15	0.73	131.7
		3D-FB	52.7	46.3	0.128	5.48	9.79	11.46	22.7	0.18	0.95	137.9
		IMRT-DIBH	53.7	45.2	0.170	3.20	3.33	9.45	18.3	0.15	0.20	137.4
		TD-FB	51.2	47.5	0.075	2.85	3.49	7.32	14.3	0.26	1.99	138.9

Abbreviations: ID: integral dose. HI: homogeneity index. $D_{2\%}$, $D_{98\%}$: dose encompassing 2% and 98% of the volume respectively. V_{20Gy} (%): volume receiving 20 Gy. TD-FB: TomoDirect in free-breathing. 3D-FB: 3D conformal radiotherapy in free-breathing. 3D-DIBH: 3D conformal radiotherapy in deep inspiration breath-hold. IMRT-DIBH: intensity modulated radiotherapy in deep inspiration breath-hold.

($D_{98\%}$ = 46.9 to 47.2 Gy, $p < 0.001$). In addition, near-maximum dose is lower for TomoDirect ($D_{2\%}$ = 51 Gy) than for 3DCRT and IMRT ($D_{2\%}$ = 52.6 to 53 Gy, $p < 0.001$), with no impact from DIBH.

PTV homogeneity is significantly better for TomoDirect than for IMRT. This ability of TomoDirect to produce a more homogeneous target dose has already been observed for breast treatments relative to static IMRT [10] and 3DCRT [11,18]. This significant improvement in the homogeneity of the dose may result with potential improvements in cosmetic outcome [19], even if a beneficial effect on quality of life remains to be demonstrated [20].

Static IMRT is deemed able to improve PTV homogeneity compared to 3DCRT [8,21]. Yet, like many other authors [10,22,23], we did not observe significant difference between 3DCRT and IMRT techniques. The main hypotheses is in our opinion that our 3DCRT technique can compensate very effectively over and underdosages, by the use of wedge filters, MLC field in field or beam weights.

Right breast, right lung and patient

The averaged maximum dose to the right breast is less than 2.8 Gy for all techniques. We took care not to irradiate the contralateral breast with a direct beam when planning, so it is not surprising that we found no significant difference between the 4 modalities studied. Equivalent results were published for various dosimetric comparisons [8,10,24].

The mean right lung dose varies from 0.12 to 0.25 Gy, depending on the technique. It is statistically higher with TomoDirect and lower with IMRT-DIBH ($p < 0.001$). However, given the very low dose values, it is very unlikely to have any clinical impact.

The risk of radiation-induced cancer may increase with the integral dose to the patient [25]. In our study, the lowest ID is obtained with breath-hold, with a significant gain of about 5% compared to free-breathing techniques. Remember that TomoDirect plans have been calculated without the Dynamic Jaw option, which can potentially reduce ID by 9% [26]. We observe no link between IMRT and ID: our results are in line with those of Olch [27] and Abo-Madyan [28], who concluded that IMRT do not necessarily increase the ID, and that the risk of second cancers for breast irradiation are equivalent for tangential fields, regardless of the technology (3DCRT or IMRT).

Left lung

TomoDirect is the best technique to spare the left lung, despite the lack of respiratory gating: TD-FB reduces the average dose to the left lung respectively by 35%, 24% and 32% compared to 3D-FB, 3D-DIBH and IMRT-DIBH. Similar values are obtained for the V_{20} and comparable results can be found in the literature [10,11,18].

We found no benefit to use IMRT-DIBH rather than 3D-DIBH to reduce ipsilateral lung dose, as also observed by Ashraf [22]. However, other authors showed that IMRT can reduce the average dose to the left lung from 7 to 19% compared to 3DCRT [10,12,23]. These discrepancies may be explained by the modest values found in the literature, often at limit of significance level, and by planning techniques that can vary according to the authors.

When comparing 3DCRT with and without breath-hold, we found that DIBH can reduce the average dose to the left lung by 14% (p = 0.007), which is comparable to some results 7 to 28% in the literature [5,17,29]. However, several publications show no significant effect of the DIBH technique on pulmonary sparing [30]. These discrepancies may again find their origin in the various planning techniques, and in the modest values of lung dose reductions obtained with respiratory gating.

What is the best technique?

TomoDirect can only operate in free breathing: is it an insurmountable handicap for the treatment of the left breast, or is the TomoTherapy modulation capable to compensate for the lack of respiratory gating? To our knowledge, no study had yet compared TomoDirect with breath-hold techniques.

The lack of gating in TomoDirect is detrimental to some patients for whom DIBH remains essential for cardiac sparing. Nevertheless, the average gain to the heart obtained with DIBH remains relatively small, and significant dose differences are achieved only for a limited number of patients. For PTV dose homogeneity and left pulmonary dose, TomoDirect can achieve better plans than 3DCRT and IMRT, with or without DIBH.

Thus, it seems to us that the TomoDirect technique is complementary to a 3DCRT technique with DIBH. For a minority of patients, breath-hold should be used if the cardiac dose reduction is a priority over PTV homogeneity or left pulmonary dose. For the majority of the remaining patients, TomoDirect achieves similar cardiac dose than the one obtained with 3DCRT or IMRT with respiratory gating, with a significant reduction in the left pulmonary dose and an improvement of PTV homogeneity. Use of Dynamic Jaw option remains then mandatory to reduce the integral dose to the patient.

Incidentally, our results show as many other studies that DIBH reduces the dose to the heart compared with a 3DCRT technique without DIBH. We are much more reserved about the contribution of static IMRT with DIBH, whether for the heart, the left lung or the

Appendix 3
Detailed AIC statistical analysis results.

	Log-transformed?	Best-model	$F_{3,42}$	p-Value for best-model effect
PTV				
$D_{2\%}$ (Gy)	No	Technique only	55.18	<0.001
$D_{98\%}$ (Gy)	No	Technique only	10.43	<0.001
HI	Yes	Technique only	42.45	<0.001
Heart				
D_{mean} (Gy)	No	Technique only	28.75	<0.001
V_{20Gy} (%)	No	Technique only	29.40	<0.001
Left lung				
D_{mean}(Gy)	No	Technique only	26.20	<0.001
V_{20Gy} (%)	No	Technique only	24.18	<0.001
Right lung				
D_{mean} (Gy)	No	Technique only	65.05	<0.001
Right breast				
D_{max} (Gy)	Yes	Technique only	0.422	0.738
Patient				
ID (Gy cm^3)	No	Technique and breast volume	7.294	<0.001

Abbreviations: ID: integral dose. HI: homogeneity index. $D_{2\%}$, $D_{98\%}$: dose encompassing 2% and 98% of the volume respectively. V_{20Gy} (%): volume receiving 20 Gy.

PTV dose homogeneity: an efficient 3DCRT technique with respiratory gating may be sufficient.

Conclusion

For a small number of patients treated for left breast radiotherapy, lack of respiratory gating in TomoDirect is a handicap for the cardiac dose. However, the sparing of the left lung and the PTV dose homogeneity are routinely better for TomoDirect than for 3DCRT with deep-inspiration breath-hold. Free breathing TomoDirect and breath-hold 3DCRT treatments are therefore complementary: for a minority of patients, respiratory gating remains mandatory if cardiac dose is a priority; for the remaining majority of patients, TomoDirect helps to achieve better PTV homogeneity and reduced left lung dose, with cardiac dose equivalent to that obtained for 3DCRT with breath-holding.

Appendix A

See Appendices 1–3.

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