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Scientific Article

Dosimetric Comparison of CPAP and DIBH for Left-sided Breast Cancer Radiation Therapy

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Purpose: Despite the increasing interest in using continuous positive airway pressure (CPAP) in radiation therapy (RT), direct comparisons with the more widely used deep inspiration breath-hold (DIBH) have been limited. This planning study aimed to offer comprehensive geometric and dosimetric evidence by comparing CPAP and DIBH-based RT plans.

Materials and Methods: A retrospective data set of 35 patients with left-sided breast cancer with planning computed tomography scans under three breathing conditions (free breathing (FB), CPAP with 10 cmH_2O pressure, and DIBH) was collected. Volumetric arc therapy plans aimed for 95% dose coverage to 95% of the planning target volume with a maximum dose below 107%. A comparative dosimetric analysis among the three plans was conducted. Additionally, geometric differences were assessed by calculating the minimum distance between the heart and the clinical target volume (CTV) in each planning computed tomography.

Results: CPAP and DIBH plans demonstrated comparable mean heart doses (1.05 Gy), which were significantly lower than the FB plan (1.34 Gy). The maximum dose to the left anterior descending artery was smallest in the CPAP plan (4.44 Gy), followed by DIBH (4.73 Gy) and FB (7.33 Gy) plans. Other organ-at-risk doses for CPAP and DIBH were similar, with mean contralateral breast doses of 2.27 and 2.21 Gy, mean ipsilateral lung doses of 4.09 and 4.08 Gy, V20 at 6.11% and 6.31%, and mean contralateral lung doses of 0.94 and 0.92 Gy, respectively. No significant difference was found in the minimum heart-to-CTV distance between CPAP and DIBH. DIBH exhibited the greatest lung volume (3908 cc), followed by CPAP (3509 cc), and FB(2703 cc).

Conclusions: The comparison between CPAP and DIBH shows their similarity in both geometric and dosimetric aspects, providing strong evidence for CPAP's effectiveness and feasibility in RT. This suggests its potential as an alternative to DIBH for patients with left-sided breast cancer.

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Introduction

For patients with left-sided breast cancer, the mean heart dose received during radiation therapy (RT) is reported to be associated with an increased risk of mortality.[1] This effect is higher than that for right-sided breast cancer because of the closer proximity of the heart.[2] This risk becomes more pronounced during long-term follow-ups, particularly those after 15 years.[3,4] As most patients with breast cancer become long-term survivors, managing the heart dose has been a priority during the planning and delivery of RT, particularly for left-sided breast cancer.

The breath-hold technique is one of the main approaches to minimize the heart dose during left-sided breast RT. Among various breath-hold techniques, the deep inspiration breath hold (DIBH) has gained widespread acceptance and usage. During DIBH RT, the patient inspires to a specified threshold and holds breath at every cycle of beam delivery. As a result, the expansion of the lungs and chest wall leads the heart to be displaced away from the target volume which also reduces the movement of the target caused by respiratory motion.[5] Previous studies using DIBH, including its use in conjunction with volumetric-modulated arc therapy (VMAT) and 3D-conformal radiation therapy (CRT), have consistently demonstrated a reduction in the dose delivered to the heart.[6]

Continuous positive airway pressure (CPAP), initially developed for patients with sleep apnea, has emerged as another respiration management technique for RT. CPAP provides positive pressure to the patient's airways and thereby separates the heart away from the high-dose region, offering similar anatomic outcomes to DIBH. After the initial studies that concentrated on comparing CPAP with free breathing (FB) and assessing its reproducibility,[7-13] using CPAP in RT has been recognized for its feasibility and has now entered the phase of prospective clinical trials. In the prospective study, Jacobson et al investigated the effects of CPAP on chest anatomy and tumor motion in patients receiving thoracic RT and found that CPAP provided significant volumetric and dosimetric benefits, reducing lung and heart toxicity risks while being well-tolerated by most patients.[14] More recently, Veken et al compared the positional reproducibility and dosimetric outcomes of CPAP-enhanced DIBH with surface-guided DIBH in a randomized controlled trial and determined that CPAP-assisted DIBH is non-inferior to surface-guided DIBH.[15]

However, there has been a lack of studies directly comparing the individual effects of CPAP and DIBH in a head-to-head manner which would provide critical evidence to support the role of CPAP in RT settings and provide insight into why CPAP might be advantageous. Therefore, the objective of this study was to compare the heart-sparing capabilities of CPAP and DIBH, considering both dosimetric and geometric factors, including the heart and its substructures.

Methods and Materials

Data characteristics

This study comprised a cohort of 35 patients who received a diagnosis of left-sided breast cancer, and who received treatment at Gangnam Severance Hospital. The retrospectively collected patient data included three types of simulation computed tomography (CT) based on different breath management: FB, CPAP, and DIBH (Institutional Review Board approval no. 3-2023-0233, Gangnam Severance Hospital). The patients previously underwent RT using one of the three simulation CT scans. The scan was selected by the treating physician based on visual inspection of the heart's separation from the clinical target volume (CTV) as well as patient tolerance. All patients had undergone partial mastectomy followed by whole breast irradiation. In this planning study, the target volume was the whole breast without boost, with a mean breast volume of 854.3 cc (range, 358.3-1866.4 cc). The pressure used for CPAP simulation was 10 cmH_2O for most patients. Among the 35 patients, six were excluded because of the presence of breast implants or metal that caused significant density differences, leaving 29 cases for planning and analysis.

Contour delineation

The contours required for the planning were first generated by using a deep learning-based commercial autocontouring software OncoStudio (OncoSoft Inc., Seoul, South Korea).[16] The autocontouring model uses a convolutional neural network and was trained based on contour labels that followed European Society for Radiotherapy and Oncology guidelines.[17] For every patient, the simulation CTs were all fed into the contouring workflow, and the resulting contour sets were checked and modified by a single experienced radiation oncologist. The structures of interest in this study were the CTV, as well as organs-at-risk (OARs) including the heart, left anterior descending artery (LAD), ipsilateral lung, contralateral lung, contralateral breast, and ring. A ring structure was a postprocessed structure that was expanded by 0.1 cm in all directions from CTV to ensure a more conformal dose distribution around the target.

VMAT planning

The VMAT plans with three breath management techniques were generated using RayStation (RaySearch Laboratories AB, Stockholm, Sweden) by a single observer and approved by an experienced dosimetrist. To ensure the fairness between the three VMAT plans and eliminate bias, the following planning guidelines were strictly followed, and each plan was independently generated in random orders for each patient. With the dose fractionation schedule of 40.05 Gy in 15 fractions, all plans shared a common optimization goal, with the target set to receive 95% of the prescribed dose within 95% of the planning target volume, and the maximum dose was limited to less than 107%. Dose fall-off constraints were implemented in the ring region to penalize the dose above the two dose levels D_H and D_L, which were applied for high and low dose regions, respectively. After achieving the target coverage,OAR dose optimization was performed following the ranking of the dose constraints in Table 1. Our primary focus was to minimize radiation exposure to the heart structures, including the heart and LAD. The optimization proceeded sequentially based on the rank while maintaining the dose achieved for the target and higher-ranked OARs. For the heart structures and contralateral lung, equivalent uniform dose constraints were included to consider the biologic effects of radiation.

Minimum OAR-to-target distance measurement for geometric comparison

The calculation of the geometric measure of distance between the OAR (heart and LAD) and CTV was performed using MATLAB (MathWorks). Each of the OAR and CTV contours can be defined as a set of points (X_{OAR} and X_{CTV}). The minimum OAR-to-target distance D was defined as a Euclidean norm as described in Equation 1.

$$D = \min_{x_{OAR} \in X_{OAR}} \left\{ \min_{x_{CTV} \in X_{CTV}} \{ \| x_{OAR} - x_{CTV} \|_2 \} \right\} \quad (1)$$

where x_{OAR} and x_{CTV} represent 3-dimensional coordinates, which are contained in the OAR and CTV point sets, respectively. For each OAR contour point, we computed the Euclidean distances to all CTV voxels, retaining the smallest distance. Once all iterations were finished, this established the shortest distance between OAR coordinates and CTV. Finally, the minimum value of these distances was calculated, representing the minimum OAR-to-target distance.

Treatment time comparison and statistical analysis

To comment on the impact on clinical procedures, estimates of the time taken to complete DIBH- and CPAP-based treatments were compared. At our institution, two-arc VMAT treatments require at least three to five DIBH cycles for pretreatment cone beam CT imaging and 10 to 12 for treatment. A typical DIBH cycle begins with the patient holding their breath for 10 seconds, followed by 10 to 20 seconds of relaxed breathing. As CPAP does not require breath hold, the beam-on time of the treatment was measured. The overall time excluding the set-up and training time was compared between DIBH and CPAP. The minimum OAR-to-target distance and dosimetric measures were compared between CPAP, FB, and DIBH using a paired t-test wherein $P < .05$ was considered statistically significant. The statistical analysis was computed using MATLAB.

Results

Out of the 29 patients included in this study, approximately 90% (26 patients) performed best with CPAP

Table 1 List of dose constraints used for generating VMAT plans

Structure	Type	Rank	Objective
CTV	Target	1	D95% >40.05 Gy D2% <107% D_{min} >39.55 Gy
Ring	Target	1	D_{max} <39 Gy Dose fall off (D_H) = 40.05 Gy Dose fall off (D_L) = 30 Gy
Heart	OAR	2	Maximum EUD = 3 Gy
LAD	OAR	3	Maximum EUD = 10 Gy
Ipsilateral lung	OAR	4	V20 Gy <10% V10 Gy <20% V3.5 Gy <40%
Contralateral breast	OAR	5	D_{max} <20 Gy V5 <10%
Contralateral lung	OAR	6	Maximum EUD = 5 Gy

Abbreviations: CTV = clinical target volume; EUD = equivalent uniform dose; LAD = left anterior descending artery; OAR = organ-at-risk; VMAT = volumetric arc therapy.

Table 2 Summary of dosimetric parameters computed from CPAP, DIBH, and FB-based plans

	CPAP	DIBH	FB	*P* value		
				CPAP vs DIBH	CPAP vs FB	DIBH vs FB
Mean heart dose (Gy)	1.05* (−21.64)	1.05* (−21.64)	1.34 (−)	.92	<.001	<.001
Maximum LAD dose (Gy)	4.44* (−39.43)	4.73* (−35.47)	7.33 (−)	.14	<.001	<.001
Mean contralateral breast dose (Gy)	2.27* (−7.35)	2.21* (−9.80)	2.45 (−)	.43	<.05	<.001
Mean ipsilateral lung dose (Gy)	4.09 (3.81)	4.08 (3.55)	3.94 (−)	.93	.17	.22
Ipsilateral lung V20 (%)	6.11 (4.50)	6.31 (7.87)	5.85 (−)	.35	.35	.11
Mean contralateral lung dose (Gy)	0.94* (−15.32)	0.92* (−17.12)	1.11 (−)	.62	<.05	<.001

Abbreviations: CPAP = continuous positive airway pressure; DIBH = deep inspiration breath-hold; FB = free breathing; LAD = left anterior descending artery.
*Significantly smaller than FB.
Values inside brackets indicate the percentage of change with respect to FB.

based on the treating physician's judgment and thus were treated with CPAP. Only two patients underwent FB, and one underwent DIBH-based plans.. In this study, we compared each breath-hold technique from a dosimetric, geometric, and temporal perspective.

Dosimetric comparison

Overall, there was no significant dosimetric difference between the CPAP and DIBH plans for the OARs investigated in this study, as shown in Table 2. The mean heart dose (MHD) was comparable between CPAP and DIBH (1.05 Gy) without any significant difference. The maximum LAD dose was the lowest for CPAP-based plans where the difference was only statistically significant compared with FB. The mean contralateral breast doses for CPAP and DIBH were comparable at 2.27 and 2.21 Gy, respectively. The mean contralateral lung dose was determined to be lowest with DIBH (0.92 Gy), which showed no significant difference compared with CPAP but was significantly lower than in FB. The mean ipsilateral lung dose, on the other hand, was the lowest at 3.94 Gy using FB, but there were no significant differences with the other methods.

Geometric comparison using the minimum voxel-wise distance between OAR and CTV

The displacement of the heart and the lungs varied between different techniques, as indicated by Fig. 1

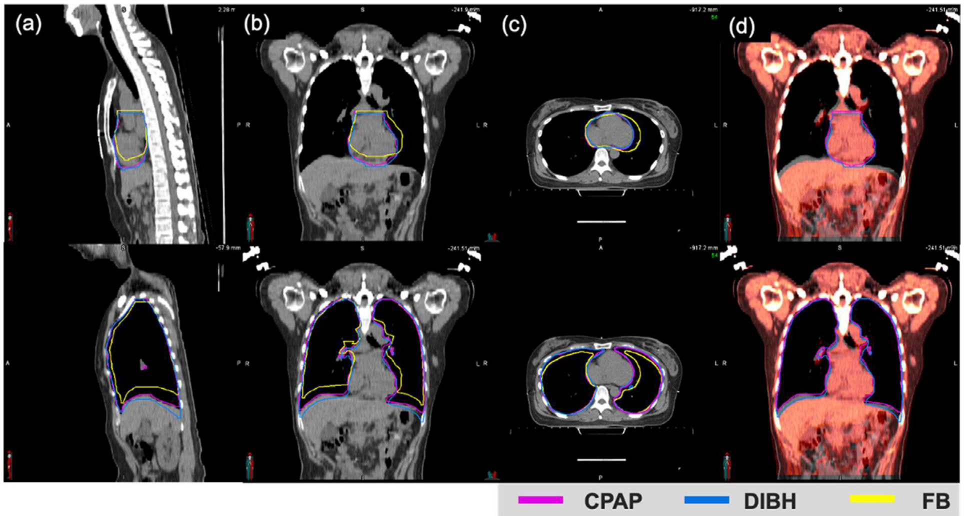

Figure 1 An example case showing heart (top row) and lung contours (bottom row) of CPAP, deep inspiration breath-hold, and free breathing scans on (a) sagittal, (b) coronal, (c) axial views on the CPAP CT and (d) fusion of the CPAP (gray) and deep inspiration breath-hold planning CT scans (red). Contour labels are colored according to the technique, as shown in the legend. *Abbreviations:*CPAP = continuous positive airway pressure;DIBH = deep inspiration breath-hold; FB = free breathing.

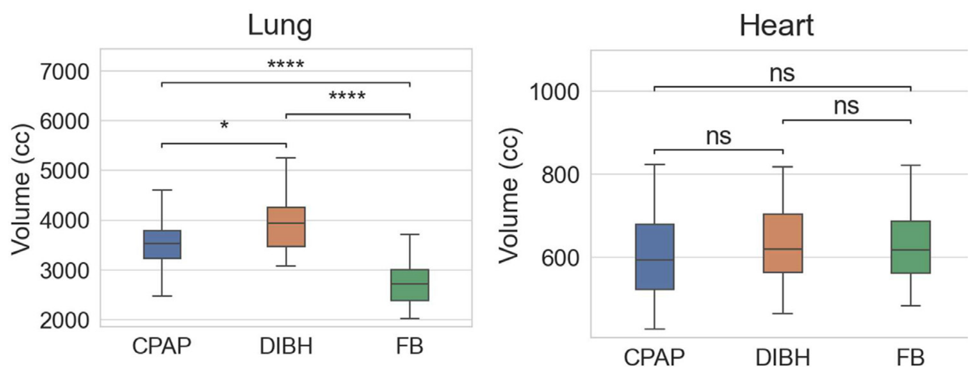

Figure 2 Comparison of lung and heart volumes in CPAP, DIBH and FB planning CT scans. Statistical significance was found pairwise where an asterisk (*) indicates statistical significance ($P < .05$), asterisks (****) denote very strong statistical significance ($P < .0001$), and ns denotes not statistically significant. *Abbreviations:* CPAP = continuous positive airway pressure; DIBH = deep inspiration breath-hold; FB = free breathing.

Table 3 Summary of mean and standard deviation of the minimum OAR-to-target surface distance in centimeters

Structure	Minimum OAR-to-target surface distance (cm)		
	CPAP	DIBH	FB
Heart	1.01 ± 0.36*	0.97 ± 0.36*	0.56 ± 0.25
LAD	1.39 ± 0.57*	1.35 ± 0.47*	0.85 ± 0.34

Abbreviations: CPAP = continuous positive airway pressure; DIBH = deep inspiration breath-hold; FB = free breathing; LAD = left anterior descending artery; OAR = organ at risk.
*Significantly greater than FB.

showing a representative case selected with the median lung volume on the CPAP scan. CPAP and DIBH both resulted in a significant displacement of the heart and lungs toward the caudal direction compared with that of FB, with DIBH having a greater impact. The lung volume was significantly greater in DIBH compared with CPAP and FB ($P < .001$) as shown in Fig. 2. Compared with FB, the lung volume was increased by 29.81% in the CPAP scans and 44.58% in DIBH scans on average. The minimum OAR-to-target surface distance was found to be the greatest in CPAP for both heart and LAD, although this difference was not significant in comparison to DIBH (Table 3). These findings are consistent with the dosimetric results in which CPAP showed similar MHD and even lower maximum LAD dose than DIBH. Fig. 3 shows a correlation map of the minimal surface distance between the heart, LAD, and their associated OAR doses. A strong correlation was found between the minimum OAR-to-target distance and the maximum LAD dose only for the CPAP-based plans. The plot indicates that, up to a certain distance, the MHD and maximum LAD dose from CPAP is slightly higher than that from DIBH, after which the effect reverses.

Time comparison between DIBH and CPAP

The median time of a typical CPAP and DIBH-based treatment was 110 and 385 seconds, respectively. DIBH involved multiple short breath holds throughout the treatment with the median number of cycles between 13 and 17 cycles, and each hold requiring 20 to 30 seconds. In contrast, CPAP does not necessitate breath holding and, consequently, did not require additional time beyond the beam-on time.

Discussion

To the best of our knowledge, this is the first planning study comparing the dosimetric impact of using CPAP and DIBH techniques for patients with left-sided breast cancer. We demonstrated that although DIBH resulted in a significantly greater lung expansion, CPAP exhibits a comparable ability to separate the heart from the target and offers similar heart dose sparing capability as DIBH. These results are of particular importance because, in this study, CPAP was used with a relatively low pressure (10 cmH_2O), possibly indicating a more improved performance with a higher pressure. Furthermore, the correlation between the organ dose and OAR-to-target distance found in this study (Fig. 3) demonstrates that CPAP has a steeper dose-to-distance relationship than DIBH. This initial outcome suggests that, for patients with an equivalent minimum OAR-to-target distance, those treated with a CPAP-based plan may experience lower organ doses than those treated with DIBH. However, further investigation is necessary to comprehend the underlying reasons for this discrepancy. Nonetheless, our research adds to earlier CPAP investigations by extending on the comparative analysis solely against FB. Allen et al previously focused on the geometric and dosimetric benefits

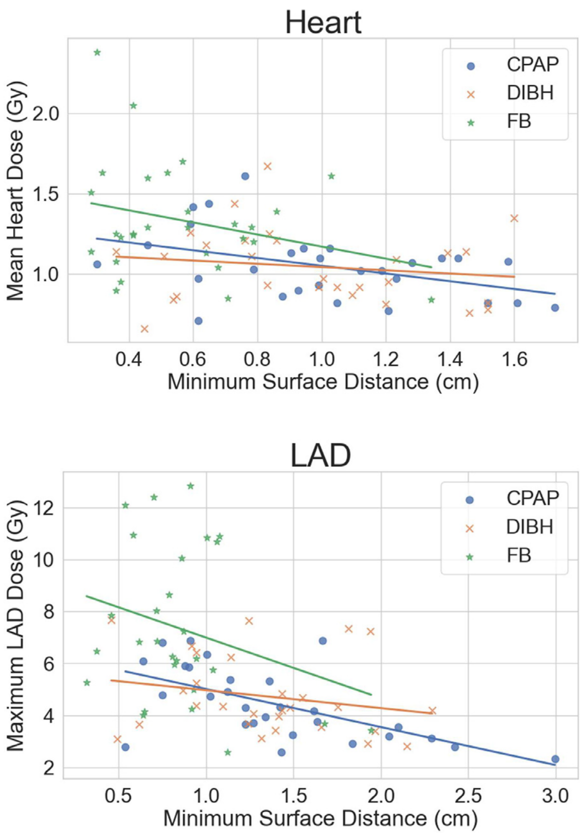

Figure 3 Correlation between organ at risk dose and minimum organ at risk dose to clinical target volume target distance of the heart and LAD. For the heart, Pearson correlation coefficients were −0.42 (P = .03), −0.16 (P = .42), and −0.27 (P = .16) for CPAP, DIBH, and FB. For the LAD, values were −0.60 (P < .01), −0.22 (P = .26), and −0.27 (P = .17) in the same order. *Abbreviations:* CPAP = continuous positive airway pressure; DIBH = deep inspiration breath-hold; FB = free breathing; LAD = left anterior descending artery.

of CPAP compared with FB within the context of 3D-CRT. Their findings revealed a caudal shift in heart position and no significant reduction in lung dose with CPAP. However, they did observe a substantial decrease in MHD (FB, 2.45 Gy; CPAP, 1.34 Gy) and heart V2.5 (FB, 19.51%; CPAP, 7.9%). Expanding upon this foundational study, we further corroborated these results with the inclusion of DIBH.

On top of the dosimetric benefits, CPAP also offers clinical advantages compared with DIBH, such as improved patient compliance and reduced need for clinical resources. Within our patient cohort, CPAP was chosen for most of the patients because it was favored by them, and its heart-sparing capability was evaluated as similar to that of DIBH. This aligns with the findings of our recent study, where 93% of patients demonstrated better tolerance toward CPAP.[13] Moreover, CPAP has been reported to be used in challenging cases where the administration of DIBH was hindered by severe lung conditions.[9] Furthermore, although DIBH demands extra efforts and training on the patient's end, CPAP offers better comfort without the need for additional training. This approach particularly benefits patients who struggle with communication and compliance issues. In terms of clinical resources, CPAP can potentially shorten treatment times by 4 times less (110 s vs 385 s per patient) because there is no need to pause or wait for patients to achieve a deep breath-hold state. This increased efficiency can be beneficial to the clinic, streamlining the RT workflow.

In comparison to other studies, our study demonstrated relatively lower MHD. A prospective study by Jacobson et al reported a decrease in MHD with CPAP, achieving 9 Gy compared with 10 Gy in FB.[14] Veken et al who investigated the effect of mechanical ventilator-assisted DIBH reported an MHD of 1.3 Gy and a maximum LAD dose of 7.7 Gy which was significantly reduced compared with conventional surface-guided DIBH.[15] Similarly, other studies using CPAP-DIBH, conducted by Reckhow et al reported an MHD of 2.5 Gy.[18] Despite separately analyzing CPAP and DIBH, our study achieved lower dosimetric outcomes, which can be explained by the fact that our study used VMAT. It can be beneficial to explore whether implementing a combined CPAP-DIBH method with VMAT may further reduce dosimetric outcomes. Nonetheless, our findings indicate that CPAP alone led to notable reductions in heart and LAD doses. This result highlights the potential benefits for patients who are unable to undergo DIBH, even when assisted by CPAP.

This study has a few limitations. First, the CPAP pressure used in our study was relatively low, around 10 cmH_2O, whereas previous study has indicated that higher CPAP pressures may be associated with greater lung expansion.[8] Given that a 3D-CRT-based study with a goal CPAP pressure of 15 mmHg (20.4 cmH_2O) revealed a low MHD of 1.34 Gy,[11] conducting the proposed analysis with higher CPAP pressure settings may reveal even more favorable outcomes. Second, this was a planning study and not an assessment of actual treatment plans received by patients. Although a single observer carried out the planning process, some degree of bias may exist. Additionally, the planning parameters used in this study were set uniformly for all patients, which resulted in the exclusion of extreme cases involving breast reconstruction or metallic implants. However, the objective of this planning study was to keep the settings as fair as possible for all patients to provide a fair comparison between CPAP and DIBH and thus serve as a baseline study. Exploring patient-specific planning criteria could be valuable in the future.

Conclusion

Our study demonstrated that CPAP and DIBH-based plans yield comparable dosimetric outcomes in patients with left-sided breast cancer. This finding was also consistent in the geometric analysis, revealing similar minimum distances between the OAR and the CTV. Hence, CPAP could be useful for patients who are unable to tolerate DIBH and for clinics with limited resources.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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