



## Dosimetric comparison of dual arc- volumetric modulated arc therapy (DA-VMAT) and seven-field inverse intensity modulated radiotherapy (IMRT) applied in the curative treatment of cervical cancer

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### ABSTRACT

**BACKGROUND:** In cervical cancer radiotherapy, it was aimed to compare the intensity of the dose given to the tumor volume, the maximum amount of protection of critical organs and healthy tissues, the duration of treatment in monitor unit (MU) the homogeneity and conformity indices using seven field intensity modulated radiotherapy (IMRT) and dual arc-volumetric modulated arc therapy (DA-VMAT) techniques.

**METHODS:** Fifteen patients with cervical cancer diagnosed and treated curatively, who are in stage IIB according to FIGO staging, were planned with IMRT and VMAT techniques as 50 Gy/25 fractions, and a dosimetric comparison was made in terms of target volume and organs at risk.

**RESULTS:** In terms of critical organs while the average value of the volume percentage that received 40 Gy dose for the bladder was 57.5 % in the plans made with the IMRT technique, it was found to be 50.1% in the plans made with the VMAT technique ( $p<0.07$ ). Although statistical significance could not be reached, it was observed that the protection of the VMAT technique for the intestine

was relatively higher than the IMRT technique. A statistically significant difference was found in the MU produced per fraction, and the MU value of the VMAT technique was lower than the IMRT technique ( $p<0.001$ ).

**CONCLUSION:** DA-VMAT treatment technique for cervical cancer radiotherapy at low and high doses, has intestinal protection with low MU value in VMAT technique is seen as an advantage in terms of patient comfort and device performance.

### INTRODUCTION:

It has been seen in global studies for cervical cancer that it is the second most common type of cancer among female cancers, especially in developing countries (1). Because of the silent and rapid spread of cervical cancer, it often does not give any symptoms without gynecological follow-ups until it reaches advanced stages, and its stage cannot be understood before it progresses. Cervical cancer screening tests

are important in this regard (2). According to the current staging system of the International Federation of Gynecology and Obstetrics (FIGO), approximately 50-60% of cervical cancer patients are stage IIB - IIIB cases (3). The treatment of cervical cancer patients is based on the clinical staging defined by FIGO. While surgery is the first choice for treatment in early stage disease, chemoradiotherapy +/- brachytherapy is preferred more in advanced disease (1,4-5). In theory, delivering a higher targeted dose of radiation would potentially increase the radiation exposure of surrounding healthy tissues, while reducing the likelihood of disease relapse. This limits the delivery of higher doses to the target (4). Therefore, minimizing the exposure of critical organs while giving an adequate dose to the tumor volume is the main goal of treatment. The external pelvic dose in curative radiotherapy for cervical cancer is recommended as 45Gy-50Gy according to the National Comprehensive Cancer Network (NCCN) guideline (4,5).

Intensity modulated radiotherapy (IMRT) technique has been used more and more over the years to protect the organs at risk and reduce the risk of side effects in the treatment of locally advanced cervical cancer (1,6,7). Compared to conventional radiotherapy used before IMRT became widespread, there are advantages such as higher dose applicability, more homogeneous dose distribution within the target volume, better preservation of critical organs and normal tissue (5,8-10). Currently, two types of external radiotherapy techniques are used in clinical practice of cervical cancer: static field intensity modulated radiotherapy and volumetric modulated arc therapy (VMAT). Volumetric modulated arc therapy is an advanced form of intensity modulated radiotherapy. VMAT technique can provide higher dose compliance compared to IMRT technique. Studies on the dosimetric comparison between these two techniques

show that the VMAT technique provides an improvement in target volume and preservation of organs at risk, compared to the static-field IMRT technique in the treatment of cervical cancer (11-12). In addition, a disadvantage of static field IMRT is the long duration of treatment (9,13,14).

## **MATERIALS AND METHODS:**

### **Patient selection**

Among the patients diagnosed with cervical cancer who applied to Prof.Dr.Cemil Taşcıoğlu City Hospital between 2019-2021, 15 patients whose treatment was completed with the indication of curative treatment were included in the study. All of the patients are 30 years of age or older, FIGO stage IIB and similar in terms of tumor volumes (15). For each selected patient, a 50 Gy/25 fraction was planned retrospectively using seven field IMRT and dual arc- volumetric modulated arc therapy (DA-VMAT) techniques, and a dosimetric comparison was made in terms of target volume and organs at risk.

### **Simulation:**

Computed tomography (CT) images of all patients for simulation purposes were taken with the Toshiba Aquilium LB TM device. The patients were immobilized in the supine position, and the pelvic region between L1 and upper 1/2 of the femur was imaged with axial 3mm sections, with the feet in the gantry position. In order to ensure that the target volume and critical organs are in a similar position both in the simulation CT and during the treatment, the patients were prepared to fill the bladder by drinking 1.5 lt of water before the simulation, and the simulation preparation was made by using a laxative in the rectum and intestine.

### **Volume definition:**

GTV, CTV, PTV and critical organ volumes determined by expert radiation oncologists in accordance with the International Committee of Radiation Units (ICRU)

contouring. reports on CT images; bladder, rectum, small bowel, right and left femur were contoured.

**Radiotherapy**

Contouring was based on the radiation therapy oncology group (RTOG) guidelines for inoperable cervix IMRT **technique:**

Varian Eclipse TM (Version 10.0; Varian Medical Systems, Inc., Palo Alto, CA, USA)

treatment planning of patients with target volume and critical organs contoured, with

seven field IMRT and DA-VMAT treatment doses, 50 Gy/25 fractions with virtual planning system was designed by choosing a 6MV beam modulator. While designing the planning, RTOG-0418 gynecological cervix margin protocol was followed (16).

Critical organ doses in accordance with the protocol limited to V30 < 60% of the rectum, V45 < 35% of the bladder, V40 < 30% of the small bowel volume, and V30 < 15% of the femoral volume (17,18) (Table1).

**Table1:** RTOG-0418 Critical Organ Tolerance Doses Protocol

Bowel	V40 < 30% protocol
Rectum	V30 < 60% protocol
	V50 < 35% is acceptable.
Bladder	V45 < 35% protocol
	V50 < 35% is acceptable.
Femur	V30 < 15% protocol
	V50 = 35% is acceptable.

**Seven-Field Inverse IMRT Plans**

Virtual plans of the same 15 cervical cancer patients contoured by taking BT images, were designed using seven fields with 52° angles in the IMRT technique. The field angles are 0° 52° 104° 156° 208° 260° 312° respectively. In this technique, 6MV high-energy photon beams are used (19). The dose prescription designed for the patient is defined in the system as 50Gy/25 fractions.

Eclipse Version 10.0 was used for dose calculation of the designed plans. The most appropriate plans were prepared by repeating the plan until the target volume was 50 Gy in accordance with the RTOG-0418 protocol for critical organs (16). The compatibility of the plan with the desired one was checked from the Dose-Volume histogram. The approved plans were used in the study.

**Dual-Arc VMAT Plans**

Virtual plans of the same 15 cervical cancer patients who were contoured by taking simulation CT images were designed using the DA-VMAT technique using two arcs rotating 360° in opposite directions (179° clockwise and 181° counterclockwise). The

collimator angle is set to 30° /330° and 6MV high-energy photon beam was used in the VMAT technique.

Eclipse Version 10.0 was used for dose calculation (20). While making plans, the RTOG-0418 protocol was followed for critical organs and the target volume was

ensured to receive 50Gy. The plans were repeated until the designed plans were in the desired shape and the most appropriate plan was made. The suitability of the plan was checked over DVH. The approved plans were used for the study.

### Evaluation of Treatment Plans

The treatment plans prepared for the patients included in the study and designed

with 6MV energy were controlled with the Dose-Volume Histogram, and the numerical values of the volumetric dose received by the PTV and critical organs were statistically compared. In addition homogeneity index (HI), conformity index (CI) and monitor unit (MU) values of PTV were taken and calculated separately for IMRT and VMAT techniques.

The HI value was calculated using the following equation.

$$HI = \frac{D5\%}{D95\%}$$

Here;

- ☐ D5%: The dose covering 5% of the target volume,
- ☐ D95%: Dose covering 95% of target volume.

The CI value was calculated using the following equation.

$$CI = \frac{PTV100}{PTV} \times \frac{PTV100}{V100}$$

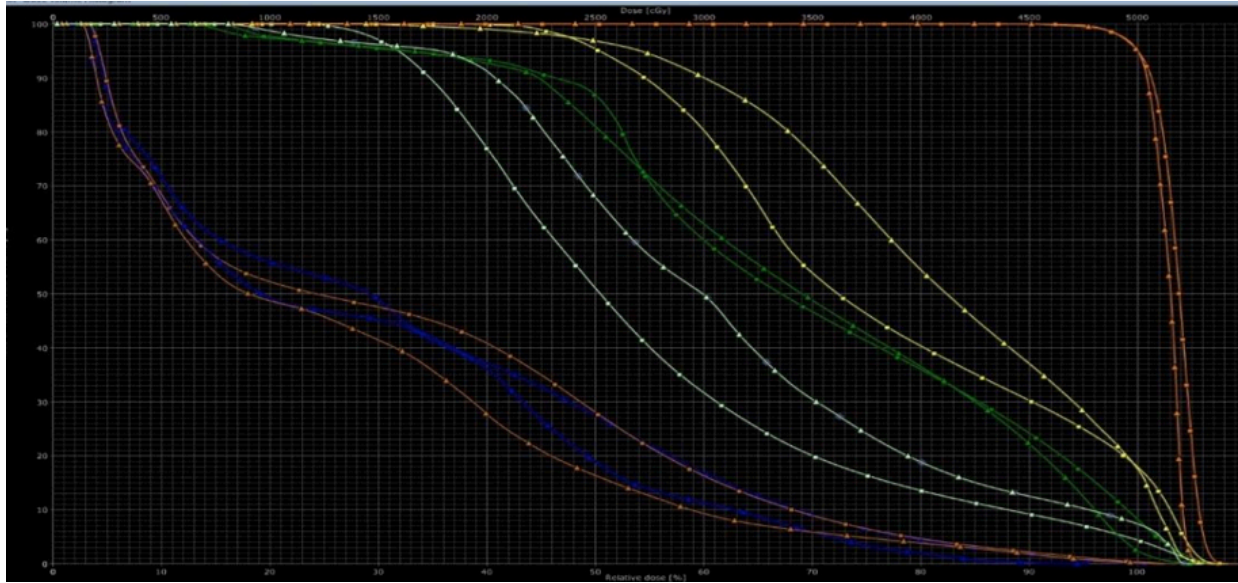
Here;

- ☐ PTV100: Volume covered by the prescribed dose
- ☐ PTV : Target volume
- ☐ V100 : Volume of the prescribed dose.

The CI and HI definitions are recommended to be used together when evaluating PTV doses by the RTOG-0418 cervical margin doses protocol, as well as by the ICRU's protocol. HI is an indicator of how homogeneously and evenly distributed the dose given for the determined PTV volume in the volume. CI is the ratio of the treated volume to the planned target volume, and both values should be close to 1 when calculated with the above formulas (8). The MU value is the value corresponding to the dose delivered by the beam from the linear accelerator. It is measured by ionization chambers located in the treatment head of linear accelerators. The MU value is

automatically calculated on the system separately for each defined field. The total MU value for the plans was calculated as the sum of the counts for each area. This procedure was applied for each patient and for both treatment techniques.

Data obtained with dose-volume histograms of treatment plans using seven field IMRT and DA-VMAT techniques were compared in terms of target volume, critical organs, as well as CI, HI, MU numbers. Figure 1 shows the DVH curves of IMRT and VMAT techniques. Here, the square shape represents the VMAT and the triangular shape represents the IMRT.



**Figure 1:** Comparison of DVHs of seven field IMRT and DA-VMAT Techniques

### Statistical methods

All data from two separate plans for each patient with IMRT and VMAT techniques were calculated with IBM SPSS Version 22 Statics. The descriptive statistics of the numerical variables obtained in the study are given as the median value. Descriptive statistics of categorical variables are given as numerical values and percentages. Considering the sample size, it was assumed that the variables were not normally distributed and non-parametric tests were used for intergroup comparisons. A significance level of  $P < 0.05$  is considered statistically significant. Man Whitney U test was used for pairwise comparisons.

### Ethical standards

For the study, Institutional permission was obtained from Prof. Dr Cemil Taşçıoğlu City

Hospital. Ethics committee approval was obtained from Istanbul Aydın University. The study was conducted in accordance with the World Medical Association's Declaration of Helsinki (5th revision, October 2000).

### RESULTS

The mean age of the patients included in the study was fifty-six. Quality control tests were carried out to check the accuracy of the plans. In all plans, PTV volume covered 95% of the prescribed dose. In the study, dose distributions of critical organs were determined with V10%, V20%, V30%, V40%, V50% values for bladder, rectum and intestine, and tolerance dose distributions for left and right femur were determined with V30% and V50% values.

The dosimetric data analyzes are shown in table 2 for critical organs.

**Table 2:** Comparison of the Doses Received by the Volumes of the Critical Organs in the Treatment Plans Made with seven field IMRT and DA-VMAT Techniques

Variable	IMRT	VMAT	P Value
	Mean $\pm$ Std. Deviation	Mean $\pm$ Std. Deviation	
Bladder %			
V10	100 $\pm$ 0	100 $\pm$ 0	1.0
V20	99.07 $\pm$ 1.37	97.94 $\pm$ 4.28	0.12
V30	89.51 $\pm$ 7.87	84.13 $\pm$ 13.76	0.493
V40	62.25 $\pm$ 13.96	53.39 $\pm$ 17.29	0.071
V50	20.8 $\pm$ 6.6	22.9 $\pm$ 11.4	0.494
Rectum %			
V10	98.04 $\pm$ 3.07	98.26 $\pm$ 2.88	0.888
V20	93.1 $\pm$ 5.81	89.95 $\pm$ 11.19	0.647
V30	78.22 $\pm$ 14.63	71.34 $\pm$ 16.34	0.245
V40	60.43 $\pm$ 17.77	49.7 $\pm$ 14.1	0.237
V50	17.38 $\pm$ 9.48	20.9 $\pm$ 11.04	0.694
Bowel %			
V10	58.88 $\pm$ 19.22	58.93 $\pm$ 19.93	0.852
V20	49.19 $\pm$ 18.84	44.59 $\pm$ 17.63	0.576
V30	29.55 $\pm$ 13.59	26.29 $\pm$ 12.43	0.372
V40	14.19 $\pm$ 6.58	13.35 $\pm$ 8.12	0.419
V50	5.06 $\pm$ 4.05	4.62 $\pm$ 3.57	0.663
Femur (left) %			
V30	11.96 $\pm$ 4.17	16.3 $\pm$ 7.7	0.065
V50	0.14 $\pm$ 0.22	0.18 $\pm$ 0.43	0.674
Femur (right) %			
V30	13.15 $\pm$ 6.36	15.76 $\pm$ 7.71	0.221
V50	0.14 $\pm$ 0.23	0.27 $\pm$ 0.75	0.941

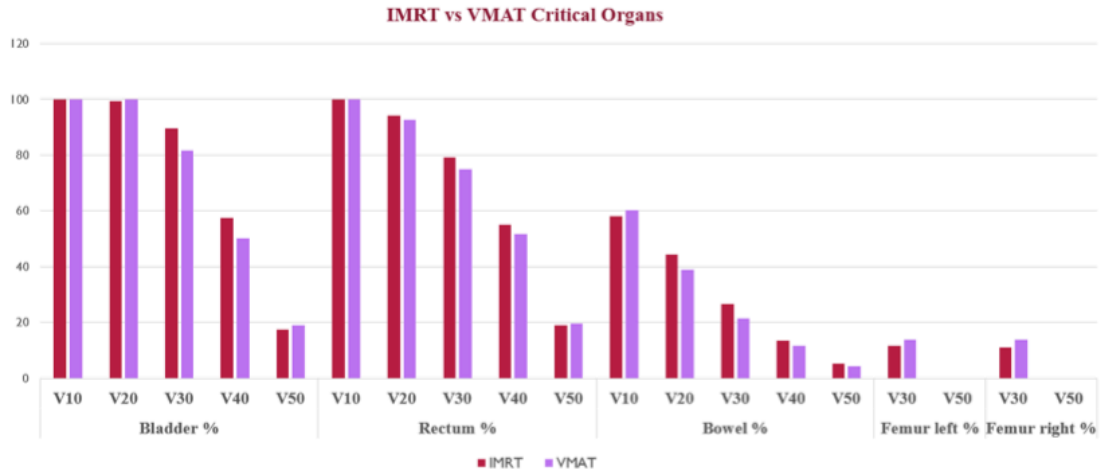
\*Man Whitney U test was used. IMRT: intensity modulated radiotherapy, VMAT: Volumetric modulated arc therapy

### Dose Distribution Data of Critical Organs:

When the data were analyzed, it was observed that the volume of the bladder receiving a dose of 40 Gy and above (V40) was 57.5% in the plans made with the seven field IMRT technique and 50.1% in the plans made with the DA-VMAT

technique ( $p < 0.07$ ). When the dose/volume parameters of the intestine were examined, although there was no statistically significant difference, it was observed that V20, V30, V40, V50 values were lower in DA-VMAT plans than IMRT (Figure 2; the pink color shows the IMRT data and the purple color shows the DA-VMAT data).





**Figure 2:** Critical Organ Comparison Chart of seven field IMRT and DA-VMAT Techniques

**Target Volume Dose Distribution Data:**

There was no significant difference between IMRT and VMAT techniques in PTVmax and PTVmin data.

On the other hand, when the PTVmean values were examined, it was seen that a

dose density closer to 50 Gy, which is the desired dose to cover the PTV, compared to the VMAT technique with the IMRT technique (PTVmean: 51.4 Gy and 52 Gy respectively,  $p < 0.012$ ). The dosimetric data analyzes are shown in table 3 for target volume parameters.

**Table 3:** Comparison of Doses Received by PTV Volumes and CI, HI, MU Values in Treatment Plans Made with IMRT and VMAT Techniques

Variable	IMRT	VMAT	P Value
	Mean±Std.Deviation	Mean±Std.Deviation	
PTVmax	5470.71±119.97	5517.7±82.31	0.178
PTVmin	4005.35±498.26	4039.37±432.89	0.52
PTVmean	5147.79±52.64	5203.1±57.98	<b>0.012</b>
CI	0.77±0.05	0.72±0.28	0.098
HI	1.06±0.02	1.06±0.02	0.539
MU	2203±284	602±88	<b>0.001</b>

\*Man Witney U test was used. IMRT: intensity modulated radiotherapy, VMAT: Volumetric modulated arc therapy

**CI, HI and MU Analysis**

The obtained data were statistically analyzed at  $p < 0.05$  significance level for seven field IMRT and DA-VMAT techniques and no significant difference was found in CI

and HI indices. However, a significant difference was found in the comparison analysis for the MU value produced by IMRT and VMAT techniques. While the MU value is 2203 in the treatment plans made with the IMRT technique, it is 602 in the treatment

plans made with the VMAT technique ( $p < 0.001$ ).

## DISCUSSION

Cervical cancer is the most common type of gynecological cancer among female cancers. However, it is in the cancer group with a high success rate of treatment with radiotherapy. Cervical cancer is a type of cancer with a high survival rate. It is of great importance to prepare treatment plans in which the small intestine, rectum, bladder, right and left femoral head, which are critical organs, will be exposed to the least possible radiation dose during radiotherapy in order to maintain the quality of life of patients for many years.

The treatment plan in radiotherapy varies according to the technique to be used. Plans for the IMRT technique are made using seven fields in cervical cancer. The reason for using seven fields is to use the angles where the critical organs will receive the least possible dose. However, this multi-field system in IMRT technique means high MU value. Thanks to the continuity of the MLC mobility in the VMAT technique, while the device rotates around the patient, the MLCs take the shape of the next area with successive movements without stopping, which significantly reduces the MU value of the treatment, while maximizing the critical organs and maximizing the dose intensity of the target volume.

In this study, seven field IMRT and dual arc-VMAT techniques were used and calculations were made with the data obtained from the treatment DVHs.

Although there is no significant difference between IMRT and VMAT for the bladder in the data obtained from the calculations, it was observed that the volume of the bladder receiving a dose of 40 Gy and above (V40) was lower with the VMAT technique. As a result of the comparative analysis of the data obtained for the intestine, no significant

difference was found between IMRT and VMAT treatment techniques.

Both treatment techniques meet the protocol requirement of  $V40 < 30\%$ . In addition, the VMAT treatment technique covered a larger volume at low doses, while at higher doses it exposed less part of the intestinal volume, providing better protection than the IMRT technique. When the doses taken by the right and left femoral heads were examined, it was observed that there was no significant difference between the IMRT and VMAT techniques, but both treatment techniques remained below the limit doses and protected the femurs. Target volume parameters PTV min, PTV max, PTV mean, CI, HI and MU values were also analyzed for both treatment techniques, and the PTV mean was found significantly higher in the VMAT technique ( $p < 0.012$ ). The IMRT technique provided a dose intensity closer to the 5000 cGy dose.

Guoa et al. applied fixed field IMRT and VMAT treatment techniques to 84 patients without lymphadenectomy and compared the techniques for target volume and critical organs. 9 fixed fields were used for IMRT plans and dual arc was used for VMAT plans. HI and CI values for VMAT plan designs were found to be superior to IMRT plan designs. It was emphasized that the number of MUs received for the VMAT technique was half the number of MUs received for the IMRT technique. A significant difference was found between VMAT and IMRT plans for the amount of dose given to the target volume. It was stated that the dose in VMAT plans in V40 of the bladder and V30 of the rectum was lower than the dose in IMRT plans.

However, it was stated that there was a similarity between the other parameters considered in the study and the clinical findings of the patients. Although the number of fields was different, a difference was observed between PTV parameters when IMRT and VMAT techniques were



compared in both studies (11). In our study, the MU value was observed to be lower in the VMAT technique compared to the IMRT technique. ( $p < 0.001$ ). VMAT technique can deliver the desired dose to the target in a short time thanks to its low MU value. However, it is more advantageous than the IMRT technique in terms of device maintenance and patient comfort.

Similarly, Qiao et al. compared IMRT and dual arc VMAT techniques, which received 5 adjuvant treatments after radical hysterectomy, and found a significant difference in MU value and CI index. The CI index is  $0.82 \pm 0.01$  for VMAT, while it is  $0.78 \pm 0.04$  for IMRT. Thus, the CI index of the plans made with the VMAT technique was observed to be better than the CI index of the IMRT plans. It was emphasized that there was no significant difference between PTV parameters and that both treatment techniques provided homogeneous dose distribution (21).

Cozzi et al. compared their plans with 5-field IMRT and single arc VMAT treatment techniques and received peripheral doses from 5, 10 and 15 cm of the PTV surface to investigate the low dose level. As a result of their study, they obtained an equivalent dose coverage result in both techniques for the target volume. They stated that the VMAT treatment technique for the HI value envelops the PTV more homogeneously and the VMAT treatment technique for the CI value gives better results than the IMRT treatment technique. It was observed that IMRT technique was higher than VMAT technique for MU values. For critical organs bladder and rectum, it has been shown that VMAT plans are more protective than IMRT plans, and healthy tissue is irradiated (20 Gy to 30 Gy) significantly less in medium and high dose regions (22).

Kang et al. compared the IMRT and dual arc VMAT techniques with 7 fields, adjusted the normalization of the PTV dose by 95% and stated that the HI value gave the same

homogeneity for IMRT and VMAT plans, but the CI value for VMAT plans was more compatible than IMRT plans. However, it was stated in the study that there was no significant difference between critical organs (23).

Zhai et al. compared the 7 field IMRT, single arc and dual arc VMAT techniques. While HI and CI values were found to be better in IMRT and dual arc VMAT techniques compared to single arc VMAT technique, there was no difference between HI and CI values in the comparison of IMRT and double arc VMAT techniques. The study found no significant difference in radiation dose to organs at risk, except the small intestine, which received  $> 40$  Gy. In addition, it was observed that single-arc and dual-arc VMAT techniques gave shorter treatment time and less MU count, and it was emphasized that this is important in terms of increasing the safety and effectiveness of pelvic irradiation (24). Treatment plans made using the VMAT technique showed an effect on protecting device health with intestinal protection and low MU value. Plans made using the IMRT technique provided a homogeneous dose density closer to 5000 cGy, which is the desired value for the PTV mean.

## CONCLUSION

In the treatment planning created for patients diagnosed with cervical cancer in line with the studies, IMRT or VMAT treatment techniques can be selected according to the suitability of the patient. There is no difference in dose homogeneity between the two techniques. However, the dual arc-VMAT technique in radiotherapy applied for the curative treatment of cervical cancer seems to provide better protection of critical organs, while at the same time having a lower MU value so it can be advantageous in terms of patient comfort and device maintenance.

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