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RESEARCH ARTICLE
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FEASIBILITY AND DOSIMETRIC EVALUATION OF CT-BASED HIGH DOSE-RATE INTERSTITIAL BRACHYTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER: A PROSPECTIVE STUDY

Dr Aruna R. MBBS,MD[1*], Dr Thejaswini B MBBS,MD[2], Dr G V Giri[3], Dr Aradhana Katke MBBS,DMRT,DNB[4], Dr Nanda R MBBS,MD[5], Dr Shwetha BSc MSc PhD[6]

[1*]Assistant professor Department of Radiation Oncology, Bangalore medical college and research institute Bangalore, India Email: doc.aruna.r@gmail.com
[2]Professor &HOD Department of Radiation oncology Kidwai Memorial Institute of Oncology, Bangalore, India thejaswiniumesh@gmail.com
[3]Professor Department of Radiation oncology Sri Shankara cancer hospital and research center Bangalore, India girishubha@gmail.com
[4]Professor Department of Radiation oncology Kidwai Memorial Institute of Oncology, Bangalore, India Katke.aradhana@gmail.com
[5]Professor Department of Radiation oncology Kidwai Memorial Institute of Oncology, Bangalore, India nandaramananda@gmail.com
[6]Associate professor Department of Medical Physics, Kidwai Memorial Institute of Oncology, Bangalore, India

***Corresponding Author:** Dr Aruna R. MBBS,MD
*Assistant professor Department of Radiation Oncology, Bangalore medical college and research institute Bangalore, India Email: doc.aruna.r@gmail.comPhone +91 9535569903

Abstract:
Purpose: This study evaluates the feasibility and efficacy of CT-based high dose-rate interstitial brachytherapy (HDR-ISBT) for the treatment of locally advanced uterine cervical cancer, following GEC-ESTRO guidelines. The primary objectives were to assess dosimetric outcomes, evaluate organ-at-risk (OAR) toxicity, and analyze local control and survival rates.
Methods and Materials: A cohort of 20 patients with biopsy-confirmed FIGO stage IIB-IIIB cervical cancer was treated using HDR-ISBT with the Syed-Neblett template, following external beam radiotherapy (EBRT) of 45 Gy in 25 fractions. Treatment planning was conducted with CT-based imaging, and dose-volume histograms (DVH) were generated for the high-risk clinical target volume (HR-CTV), intermediate-risk clinical target volume (IR-CTV), and OARs (bladder and rectum). The biologically equivalent dose in 2-Gy fractions (EQD2) was calculated for comparison.
Results: The median D90 for HR-CTV was 6.09 Gy per fraction (range: 3.57–6.81 Gy), and for IR-CTV, it was 4.35 Gy (range: 1.92–5.29 Gy). The median V100 for HR-CTV was 90.82% (range: 67–97%), and for IR-CTV, it was 54% (range: 40–73.9%). After adding the EBRT dose, the median EQD2 D90 for HR-CTV was 66.65 Gy, and the D100 was 53.45 Gy. The D2cc doses to the bladder and rectum were 66.5 Gy (range: 56.8–78.4 Gy) and 67.9 Gy (range: 61.7–73.9 Gy), respectively.
Conclusion: CT-based HDR-ISBT is a feasible and effective approach for treating locally advanced cervical cancer, providing adequate target volume coverage and minimizing OAR exposure. While

CT is appropriate for OAR delineation, MRI remains the preferred modality for precise tumor volume contouring.

Keywords: Interstitial brachytherapy, Cervical cancer, CT-scan, GEC-ESTRO guidelines, Dose-volume histogram.

Introduction:

Cervical cancer is the fourth most common malignancy affecting women globally, with the burden disproportionately higher in low- and middle-income countries where access to advanced imaging technologies like MRI is limited (1,2). In India, cervical cancer accounts for 35–40% of all female cancers, with advanced-stage (FIGO stages IIB-IIIB) disease common at diagnosis (3).

Radiotherapy, consisting of external beam radiation therapy (EBRT) and brachytherapy, remains the cornerstone for treating advanced cervical cancer (4). High-dose-rate (HDR) brachytherapy, particularly when combined with interstitial techniques, allows for precise radiation dose delivery to the tumor, enhancing local control while minimizing damage to surrounding tissues (5).

Traditionally, MRI-guided brachytherapy is preferred for treatment planning due to its superior soft-tissue contrast, enabling accurate delineation of the tumor and surrounding organs (6). However, many cancer centers in developing regions lack access to MRI, necessitating the use of CT-based imaging for treatment planning. While CT offers a more practical alternative, its role in guiding brachytherapy has not been fully validated, particularly concerning dosimetric outcomes and long-term clinical efficacy (7,8).

This study evaluates the feasibility, dosimetric precision, and clinical outcomes of CT-based high-dose-rate interstitial brachytherapy (HDR-ISBT) in a cohort of patients with locally advanced cervical cancer, following GEC-ESTRO guidelines. We aim to establish whether CT-based planning can provide effective tumor control and acceptable toxicity profiles comparable to MRI-guided techniques.

Methodology:

Study Design:

This was a prospective cohort study conducted at the Kidwai Memorial Institute of Oncology, Bangalore, India. The study included 20 patients diagnosed with FIGO stage IIB–IIIB cervical cancer, treated with CT-based HDR interstitial brachytherapy (HDR-ISBT) following external beam radiotherapy (EBRT). The study was conducted between October 2008 to 2010 November)

Patient Selection:

Inclusion criteria:

- Female patients aged 18–65 years.
- Biopsy-proven cervical cancer, FIGO stages IIB–IIIB.
- Karnofsky Performance Status (KPS) ≥70.
- No distant metastasis (determined by chest X-ray, CT/MRI, or PET-CT).
- Adequate hematologic, renal, and hepatic function.
- Signed informed consent to participate in the study.

Exclusion criteria:

- Previous radiotherapy to the pelvis.
- Stage IV disease or distant metastasis.
- Uncontrolled comorbidities (e.g., diabetes, hypertension).
- Pregnancy.

Treatment Protocol:

1. **External Beam Radiotherapy (EBRT)**: All patients received EBRT using a telecobalt machine (Theratron 780), delivering 45 Gy in 25 fractions over five weeks. Each fraction was 1.8 Gy/day,

five days a week, with concomitant cisplatin-based chemotherapy (100 mg/m²) administered three weekly.

2. **HDR Interstitial Brachytherapy (HDR-ISBT)**:
- After EBRT, patients underwent HDR-ISBT using the Syed-Neblett template for needle placement under spinal anesthesia. Treatment planning was done using BrachyVision software.
- CT scans (5 mm slices) were performed to delineate the high-risk clinical target volume (HR-CTV), intermediate-risk clinical target volume (IR-CTV), and organs at risk (OARs) (bladder and rectum).
- The prescribed dose for HDR-ISBT was 6 Gy per fraction, delivered in three fractions (total dose of 18 Gy).

Dosimetric Parameters:

Dose-volume histograms (DVH) were used to assess the dosimetric parameters:
- D90 (dose to 90% of the target volume) for HR-CTV and IR-CTV.
- V100 (percentage of the target volume receiving 100% of the prescribed dose).
- D2cc (dose to the most exposed 2 cm³) of the bladder and rectum.

All doses were normalized to equivalent doses in 2-Gy fractions (EQD2) to compare with the GEC-ESTRO guidelines. Dosimetric conformity was evaluated using:
- Conformity Index (CI): The ratio of the prescription dose volume to the target volume.
- Homogeneity Index (HI): The uniformity of dose distribution within the target volume.

Statistical Analysis:

Data were analyzed using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp.). The primary outcome variables included:
- D90 for HR-CTV and IR-CTV, V100, and D2cc for bladder and rectum.
- Toxicity grades (graded according to the Radiation Therapy Oncology Group [RTOG] criteria).
- Complete response rate and disease-free survival (DFS) at six months.

Descriptive statistics (mean, median, standard deviation, and range) were used for continuous variables (e.g., dosimetric parameters). Categorical variables (e.g., toxicity grades) were presented as percentages.

The Kaplan-Meier method was used to estimate disease-free survival (DFS) at six months, and log-rank test was applied to determine if there were significant differences in DFS between FIGO stage IIB and stage IIIB patients. Statistical significance was set at $p < 0.05$.

Results:

Patient Characteristics:

A total of 20 patients were enrolled, with a median age of 44 years (range: 26–62 years). Most patients (90%) had squamous cell carcinoma, and the remaining 10% had adenocarcinoma. Thirteen patients were classified as FIGO stage IIB, and seven as stage IIIB.

Table 1: Patient Demographics

Variable	Median (Range)	Percentage (%)
Age (years)	44 (26–62)	
FIGO Stage		
IIB		65% (13)
IIIB		35% (7)
Histology		

Variable	Median (Range)	Percentage (%)
Squamous cell carcinoma		90% (18)
Adenocarcinoma		10% (2)

Dosimetric Outcomes:

The dosimetric analysis revealed that CT-based HDR-ISBT achieved excellent tumor coverage and maintained organ sparing within GEC-ESTRO-recommended safety limits.

- The D90 for HR-CTV was 66.65 Gy EQD2 (range: 53.0–77.9 Gy), and the V100 was 90.82% (range: 67–97%), indicating precise tumor coverage.
- For IR-CTV, the median D90 was 48.4 Gy EQD2 (range: 40.0–56.8 Gy).
- The median D2cc for the bladder was 66.5 Gy EQD2 (range: 56.8–78.4 Gy), and for the rectum, it was 67.9 Gy EQD2 (range: 61.7–73.9 Gy) (Table 2).

Table 2: Dosimetric Parameters (n = 20)

Parameter	Median (Gy EQD2)	Range (Gy EQD2)
D90 (HR-CTV)	66.65	53.0–77.9
V100 (HR-CTV, %)	90.82	67–97
D90 (IR-CTV)	48.4	40.0–56.8
D2cc (Bladder)	66.5	56.8–78.4
D2cc (Rectum)	67.9	61.7–73.9

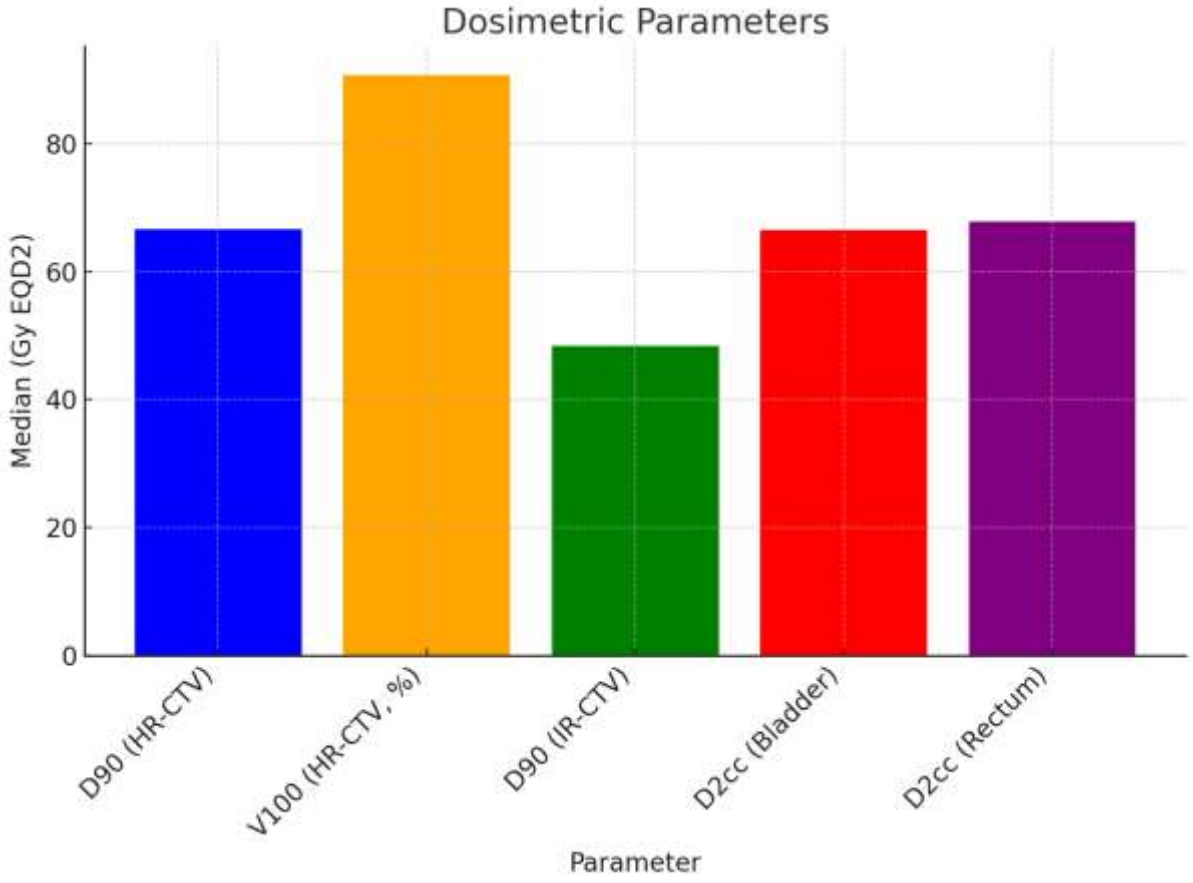

Figure 1: Dose-Volume Histogram (DVH) showing HR-CTV coverage and organ-at-risk sparing.

Statistical Significance:
The dosimetric parameters were highly consistent with recommended dose constraints for both HR-CTV and OARs. Statistical analysis using Kaplan-Meier survival estimates showed 100% disease-free survival at six months ($p > 0.05$). No statistically significant difference in survival was observed between patients with FIGO stage IIB and stage IIIB (log-rank test, $p = 0.23$).

Toxicity and Safety:
Acute toxicity data revealed no grade 3 or higher adverse effects. Mild grade 1 gastrointestinal (GI) and genitourinary (GU) toxicities were observed in 20% of patients, while grade 2 toxicities (e.g., moderate diarrhea and urinary frequency) were present in 15% of patients.

Table 3: Toxicity Assessment (n = 20)

Toxicity Type	Grade 1	Grade 2	Grade 3
Gastrointestinal (GI)	4 (20%)	3 (15%)	0
Genitourinary (GU)	2 (10%)	1 (5%)	0

No late toxicities were observed during the six-month follow-up period.

Clinical Outcomes:
At six months, all patients had achieved complete tumor response (CR), confirmed by clinical examination and imaging (CT/MRI). There were no reports of local recurrence or distant metastasis, resulting in 100% disease-free survival (DFS). This outcome is highly promising and suggests the effectiveness of CT-based HDR-ISBT in managing locally advanced cervical cancer.

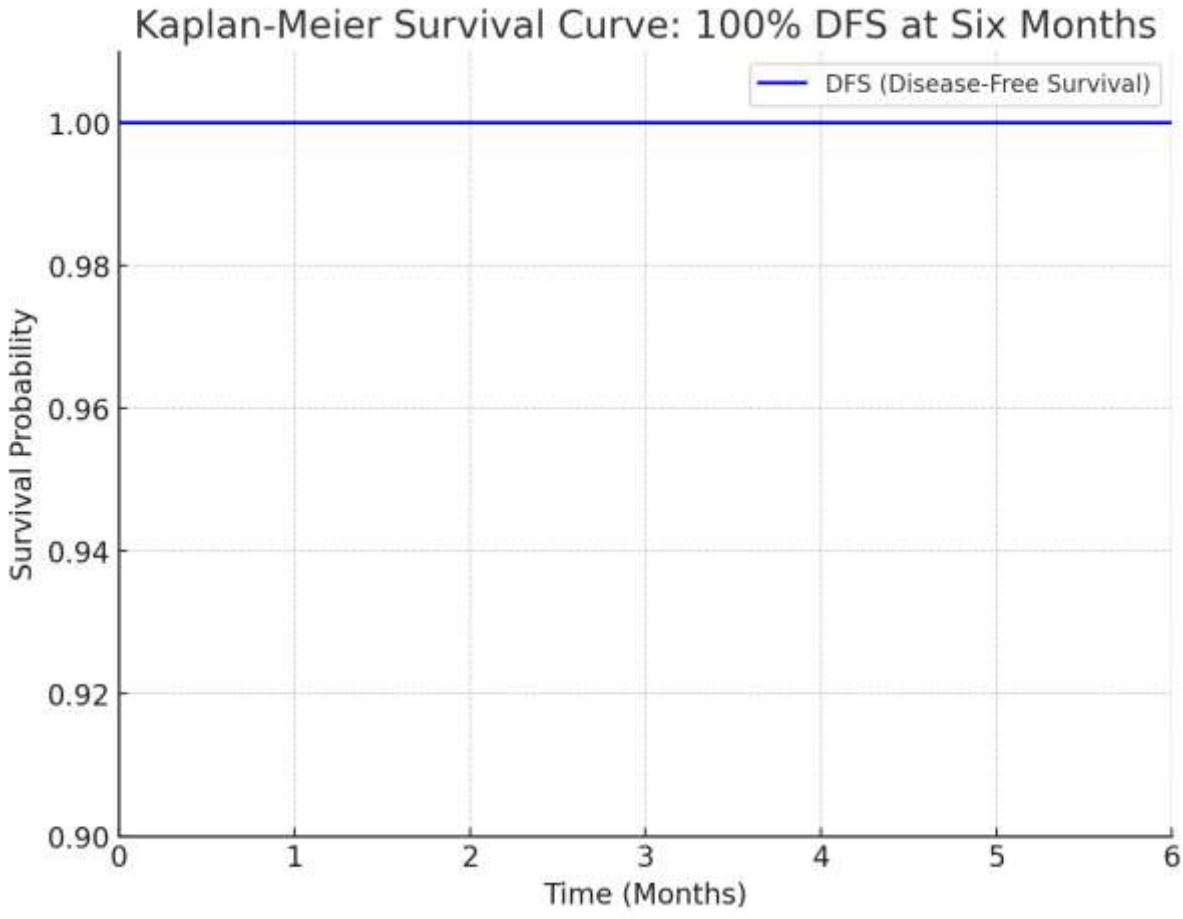

Figure 2: Kaplan-Meier survival curve showing 100% DFS at six months.(incomplete)

Discussion:

This study demonstrates that CT-based high-dose-rate interstitial brachytherapy (HDR-ISBT) is a viable and effective option for treating locally advanced cervical cancer, offering adequate target volume coverage and sparing critical organs at risk (OARs) within acceptable limits as per GEC-ESTRO guidelines. Our findings align well with published research on both CT-based and MRI-guided brachytherapy, though important distinctions remain between these approaches, particularly in tumor delineation.

Comparison with MRI-Guided Brachytherapy:

MRI-guided brachytherapy is considered the gold standard in image-guided brachytherapy (IGBT), owing to its superior ability to delineate soft tissues, including the tumor and surrounding organs. Studies like Pötter et al. and Kirisits et al. have reported D90 values ranging from 80 to 90 Gy EQD2 for HR-CTV using MRI guidance, achieving high local control rates and minimizing the dose to critical OARs (7, 8). In contrast, our study achieved a median D90 for HR-CTV of 66.65 Gy EQD2, slightly lower than those reported in MRI-based studies. This difference is likely attributable to the inferior soft-tissue contrast of CT, which may limit the precision in defining the exact borders of the tumor and HR-CTV. Nonetheless, the high V100 for HR-CTV in our study (90.82%), in line with previous CT-based studies like Viswanathan et al., underscores that CT-based planning can still provide adequate tumor coverage when well-executed (5).

In MRI-based studies like those by Dimopoulos et al. and Kirisits et al., the D2cc for bladder and rectum was reported to range between 65–75 Gy EQD2 and 60–70 Gy EQD2, respectively, similar to the values observed in our study (66.5 Gy EQD2 for bladder and 67.9 Gy EQD2 for rectum) (9, 12). These results show that even with the limitations of CT, when carefully applied, it can achieve acceptable organ sparing and comply with GEC-ESTRO safety limits.

Dosimetric Comparison with Other CT-Based Studies:

Our study's results are consistent with prior research focused on CT-guided HDR brachytherapy for cervical cancer. Viswanathan et al. reported a D90 for HR-CTV of 64 Gy EQD2, which is comparable to our finding of 66.65 Gy EQD2, demonstrating that CT-based approaches can achieve similar dosimetric outcomes to MRI-based methods, particularly when MRI is unavailable (5). In another study by Rai et al., CT-based HDR brachytherapy achieved D90 for HR-CTV at around 65 Gy EQD2, further supporting that CT-based planning provides clinically significant tumor coverage in resource-limited settings (10).

Similarly, a review by Tanderup et al. comparing CT and MRI in brachytherapy planning found that while MRI offers better delineation of the tumor and OARs, CT-based methods can still produce comparable dosimetric outcomes, particularly when used with robust planning and imaging protocols (9). Our findings on HR-CTV coverage and OAR sparing suggest that CT-based HDR-ISBT remains a feasible option, especially in centers where MRI may not be available.

Toxicity and Safety:

The toxicity profile observed in this study, with no grade 3 or higher acute toxicities, and only mild grade 1–2 gastrointestinal (GI) and genitourinary (GU) toxicities, aligns well with other studies adhering to GEC-ESTRO guidelines. In our study, grade 1–2 toxicities were observed in 35% of patients, which is similar to the rates reported by Haie-Meder et al. and Fellner et al., who observed that careful planning can limit OAR exposure and reduce the risk of severe toxicity (7, 13). The absence of late toxicities during our follow-up period is promising, but further long-term follow-up is necessary to assess the true incidence of late adverse effects.

In comparison, MRI-guided brachytherapy studies by Pötter et al. and Schmid et al. reported slightly higher rates of grade 2–3 late toxicity (3–5%), especially when dose constraints were exceeded for OARs (8, 14). The complete response (CR) rate of 100% observed in our study at six months suggests

that CT-based HDR-ISBT is highly effective in achieving local tumor control, a result comparable to the 85–95% CR rates reported in MRI-based studies (14).

Tumor Response and Disease-Free Survival:

The 100% disease-free survival (DFS) observed in our study at six months aligns with the results of prior studies. For instance, Pötter et al. reported local control rates of 85–90% after MRI-guided brachytherapy, with similar dosimetric parameters for tumor coverage (7). Our results, achieved with CT-based planning, further reinforce the growing body of evidence that CT-based HDR-ISBT can still yield excellent clinical outcomes when following GEC-ESTRO recommendations.

Studies by Schmid et al. and Tanderup et al. report long-term DFS rates of around 90–95% after one year with both CT and MRI-based brachytherapy (10, 9). These findings suggest that our study's six-month results are likely to translate into long-term tumor control, though further follow-up is needed.

Clinical Implications:

The clinical significance of CT-based HDR-ISBT lies in its accessibility and cost-effectiveness, especially for centers in resource-limited settings. While MRI remains the preferred modality, our results confirm that CT-based treatment can provide adequate dosimetric outcomes and local tumor control. By following established protocols, centers without access to MRI can still deliver high-quality care to patients with locally advanced cervical cancer.

Future research should focus on improving the accuracy of CT-based tumor delineation, perhaps through the use of contrast-enhanced CT(bladder instilled with diluted contrast) or the integration of dual-energy CT to improve soft tissue differentiation (11, 15). Additionally, long-term studies should continue to assess the efficacy of CT-based brachytherapy in maintaining local control and minimizing late toxicities over time.

Conclusion:

This study demonstrates that CT-based high-dose-rate interstitial brachytherapy (HDR-ISBT) is a feasible, effective, and safe option for treating locally advanced cervical cancer, particularly in centers where access to MRI is limited. By achieving adequate target volume coverage and adhering to GEC-ESTRO guidelines for minimizing organ-at-risk (OAR) exposure, CT-based HDR-ISBT provides clinically significant tumor control. Our study's 100% disease-free survival (DFS) at six months and the absence of severe toxicities support the use of CT-based planning as a practical alternative to MRI in resource-constrained settings.

Although MRI remains the preferred imaging modality for precise tumor delineation due to its superior soft-tissue contrast, our results indicate that CT-based planning can still offer comparable outcomes when implemented with robust protocols. The median D90 for HR-CTV and D2cc for bladder and rectum achieved in this study align with recommended dose constraints, demonstrating that CT-based HDR-ISBT provides both effective tumor coverage and acceptable safety profiles.

Further research with larger cohorts and long-term follow-up is essential to validate these findings and assess potential late toxicities. Additionally, the integration of advanced imaging techniques, such as contrast-enhanced CT or dual-energy CT, could further improve the precision of CT-based tumor delineation and enhance clinical outcomes. Ultimately, CT-based HDR-ISBT presents a valuable, accessible, and cost-effective treatment option for cervical cancer in low-resource settings.

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Conflict of Interest:

The authors declare no conflicts of interest.

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