Guidelines for Clinical Implementation of Lattice Radiotherapy for the Treatment of Unresectable Bulky Uterine Cervical Cancer

Beatriz Amendola, Naipy C. Perez, Michael Hall, Marco Amendola, Xiaodong Wu
Innovative Cancer Institute / Executive Medical Physics Associates

OBJECTIVES:
To establish a standardized protocol for Lattice Radiotherapy (LRT) for bulky locoregionally advanced uterine cervical cancer. The proposed guidelines include adequate patient selection, detailed simulation and treatment planning recommendation, and strict dosimetric parameters to be reported in order to compare data.

MATERIAL AND METHODS:
The LRT protocol is based on our experience of more than a decade of using LRT for voluminous cervical cancer and in the previously published International Consensus on the Design of prospective SFRT clinical trials for advanced gynecological cancer.


cancers MDPI

Guidelines

An International Consensus on the Design of Prospective Clinical–Translational Trials in Spatially Fractionated Radiation Therapy for Advanced Gynecologic Cancer

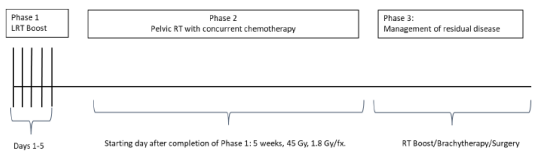
Beatriz E. Amendola [1], Anand Mahadevan [2], Jesus Manuel Blanco Suarez [3], Robert J. Griffin [4], Xiaodong Wu [5], Naipy C. Perez [1], Daniel S. Hippe [6], Charles B. Simone II [7], Majid Mohiuddin [8], Mohammed Mohiuddin [9], James W. Snider [10], Hualin Zhang [11], Quynh-Thu Le [12] and Nina A. Mayr [13,*]

RESULTS:

Patient Eligibility Criteria
- Tumor size: > 4 cm
- Non-surgical candidate
- Stage: IB3-IVA
- Histology: SCC, Adenocarcinoma, Adenosquamous carcinoma
- Tumor markers: Both HPV+ and HPV-
- Age: >18 y, no upper age limit
- Karnofsky performance status >70%

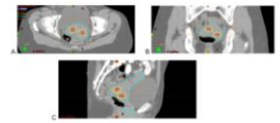
Imaging and CT simulation
- Follow SBRT Guidelines
- Oral contrast
- Neutral position, leg rest.
- Immobilization with Aquaplast mold (recommended)
- 2 mm slice thickness
- Acquire two sets of images: scan with full, comfortable bladder and empty bladder to obtain ITV. Image set with full bladder will be used for planning.
- Scan from T12 to the Ischial Tuberosity
- The use of additional diagnostic images for contouring and planning decision is highly recommended. Magnetic Resonance Imaging (MRI) is preferable, and ideally both MRI and PET-CT should be used.

Dose Prescription



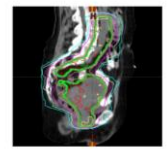
Dose Prescription Phase 1: LRT Boost

1. Peak dose in the LATTICE's vertices or Vertex Tumor Volume (VTV): $D_p \geq 8$ Gy per fraction
2. Peripheral dose in the PTV (PTV_LRT): $D_{PTV} = 2$ Gy per fraction ($D_{GTV} \leq 3$ Gy/fx)
1. Valley Dose: $D_v \leq 5$ Gy per fraction


Peak Dose (D_p) = 8 Gy per fraction (red)
Valley Dose (D_V) = 5 Gy per fraction (yellow)
Peripheral dose in the GTV (D_{GTV}) = 3 Gy per fraction (cyan)

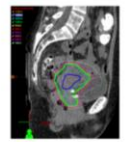
Dose Prescription Phase 2: Pelvic Irradiation

- IMRT to the pelvic lymph nodes delivered in 25 fractions of 1.8 Gy per fraction, starting the day after the completion of LRT
- If present, a simultaneous integrated boost will be administered to the PET-positive enlarged lymph nodes.
- Concurrent chemotherapy will be applied during this phase.


45 Gy, 25 fractions to the Pelvis

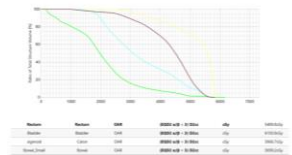
Phase 3: Management of Residual Disease

- May involve an RT Boost to residual disease, surgery, or no further treatment at the discretion of the Radiation Oncologist and surgeon, taking also into account the patient's choice and overall health status.
- To minimize additional toxicity, the para-aortic lymph nodes will be treated in a separate RT course.
- If RT Boost -> What Rx Dose?

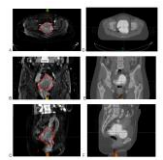

10 Gy, 5 fractions to cervix with IB of 12.5 Gy

Phase 3: RT Boost Rx

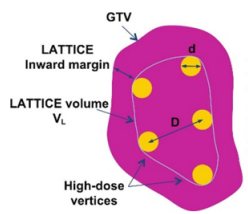
- A composite plan Dose Volume Histogram (DVH) for the first 30 fractions (Phase 1 and 2) will be obtained and evaluated. This will allow for calculating the number of fractions required in Phase 3 if an RT boost is selected. The OAR doses will not exceed 65 Gy to 2 cc of the rectum and intestines, and less than 70 Gy to the bladder.



1. Concurrent chemotherapy
2. Overall treatment time should not exceed 49 days
3. Adaptive RT will be used if necessary



Contouring



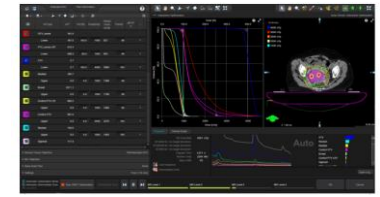
The Technical and Clinical Implementation of LATTICE Radiation Therapy (LRT)

Authors: Wu, Xiaodong, Perez, Naipy C., Zheng, Yi, Li, Xiaobo, Jiang, Liuqing, et al.

Source: Radiation Research, 194(6) : 737-746

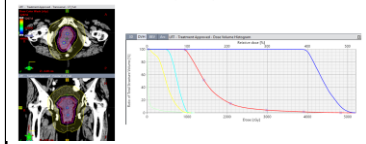
1. GTV_LRT: Macroscopic tumor as per CT and MRI. Includes the cervix gross tumor volume and the extension to the uterus and/or vagina, if present.
2. PTV_LRT: Usually includes the ITV of the GTV_LRT, uterus, and vagina with 0.5 cm margin. Prescription dose to PTV_LRT (D_{PTV}).
3. V_L: LRT Volume; Contraction of the GTV_LRT by 0.7 cm (0.5 cm ↕)
4. VTV: vertex tumor volume; group of spheres (vertices) located inside the V_L. Convert this structure to high resolution.
5. d: vertex diameter equal to 1 cm.
6. D: distance between the vertices: 2.5 cm to 3 cm in axial plane and 2 cm to 2.5 cm in sagittal/coronal plane.
7. Check VTV/GTV_LRT, should be between 0.5% to 2 %.
8. Control VTV: Structure to control the 5 Gy valley dose = GTV_LRT – (VTV + 0.5 cm, 0.3 cm up and down). The minimum axial distance to put 2 vertices is 5 cm.
9. Control PTV = Extract wall from PTV_LRT (2 cm – 0.1 cm) with the objective of maintain a good conformity in the planning target volume.

Treatment Planning/Optimization

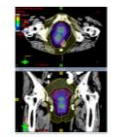


Plan Evaluation and Reporting

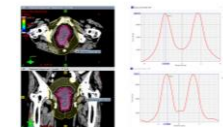
Plan Evaluation : 40 Gy, 8 Gy/fx in VTV



10 Gy (2 Gy/fx) in PTV



25 Gy (5 Gy/fx) V5 Gy < 8%
Peak-Valley distribution



	Evaluation	Expected value	Acceptable	Notes
1	Volume of the VTV receiving $D_p \geq 40$ Gy	≥95%		95% of every vertex should be covered by D_p
2	Volume of GTV_LRT receiving peripheral Dose (D_{PTV})	≥95%	≥80%	Depends on the main objective of the plan, at physician's discretion
3	Volume of PTV_LRT receiving D_{PTV}	≥90%	≥80%	Depends on the main objective of the plan, at physician's discretion
4	Volume of GTV_LRT receiving more than 5Gy per fraction	≤15%	≤30%	5 Gy isodose lines (IDL) should be completely separated one from the other in order to get an adequate peak to valley dose distribution
5	Dose in Control_VTV	≤5 Gy per fraction	≤6 Gy	
6	Dose in Control_PTV	< 0.9*D_{PTV}	< 1.1*D_{PTV}	
8	D_{2cc} of Rectum, Sigmoid Colon, and Bladder	≤D_{PTV}		In certain cases, the coverage of PTV_LRT can be intentionally compromised to lower D_{2cc} to OAR

Treatment Delivery
- The radiation oncologist and the medical physicist must be present on the first day of treatment. The radiation oncologist should review the images prior to every fraction.
- A Cone Beam Computed Tomography (CBCT) will be performed initially for patient alignment, followed by a second CBCT for confirmation
- Shifts in patient position and internal organ alignment between the first and second CBCT should be less than 1 mm
- If more than two arcs are used, a third confirmatory CBCT will be performed after delivering the second arc.

Follow-up
- First imaging follow-up will be conducted 3 months after completing the radiation therapy course, including PET-CT and MRI, if feasible, in addition to clinical evaluation
- Second follow-up will occur at 6 months and subsequent follow-ups every 6 months for the first 2 years.
- Annual visits with follow-up imaging studies are recommended thereafter.

CONCLUSIONS:
Our preliminary results of using three LRT fractions of LRT combined with chemoradiation for patients with bulky cervical cancer have demonstrated a complete tumor response of 70% with no grade 3 or 4 toxicity reported. The current protocol proposes a dose escalation using five LRT fractions as an upfront boost. The results regarding tumor control probability using this regimen are expected to be of at least 85%. Implementation of the standardized LRT protocol may lead to response rates evaluation between different institutions.