

# Role of CT Scan & PET CT in locally advanced Ca. Cervix, Maiden experience at northern hilly state of India, Himachal Pradesh

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## Abstract

CT Scan & PET CT defines disease extent and guides CRT & Post-treatment response evaluation in patients treated with definitive chemo radiation.

## Objective

To determine whether positron emission tomography-computed tomography (PET-CT) Treatment response evaluation with CT imaging of the abdomen and pelvis therapy post CRT Treatment received in women with LACC.

## Methodology

A randomized prospective trial was conducted in women diagnosed & histologically confirmed stage II B to IVA carcinoma of the cervix and were candidates for chemotherapy and radiation therapy (CRT) were assessed to CT plus PET-CT of the abdomen and pelvis or CT alone. Enrollment between 2017 and June 2020 at regional cancer centers in Shimla. The PET-CT scanners were at 3 distant diagnostic institutions in Chandigarh. The median follow-up at the time of the analysis was 36 months.

## Results

Sixty Nine patients were enrolled to 18 Pretreatment PET-CT & 21 post treatment PET-CT and CT (n = 64). The trial stopped early before the planned target because of low recruitment. Mean (SD) age was 7.472. A trend in favor of PET-CT is evident result of this trial advantage for staging and response evaluation.

## Conclusion

In our series of cervical cancer patients treated with definitive CRT, post-treatment PET findings correlate more highly with outcome than post-treatment CT scan. Despite mild hyper metabolism associated with post-treatment inflammation, PET/CT continues to be highly predictive of LR, DFS, and OS. There is a high level of evidence that FDG-PET/CT plays an essential role in the primary evaluation of cervical carcinoma, particularly in evaluating lymph nodal status and distant metastasis, contributing to precise tumor staging and changes in the therapeutic attitudes. Advances in biological images like PET/CT have a tremendous impact on the evaluation of treatment response to new therapeutic strategies.

## Introduction

Himachal Pradesh LACC is the most common gynecological malignancy contributing approximately 28.9% of all female malignancies and 14.3% overall in RCC, Shimla. The disease burden is made up mostly of patients presenting in advanced stage with bulky central disease with stages II and III contributing 75% of the total load. Treatment for locally advanced cancer of the cervix (LACC) is often with curative intent consisting of cisplatin chemotherapy and concurrent radiation therapy (CRT), external beam to the pelvis, and intracavitary brachytherapy. Computed tomography (CT) with or without Positron emission tomography (PET) imaging is attractive because of the active uptake of radiolabeled F 18 by tumor cells as demonstrated that PET was superior to CT in detecting disease in pelvic and abdominal lymph nodes. [1 & 2]

## Methods

Prospective randomized study conducted at Dept. of Radiation Oncology, Indira Gandhi Medical College, Shimla. A total of 69 patients with Stage IIA-III B carcinoma of the uterine cervix were treated with CRT between 2017 and 2020. The median patient age of the patients was 47 years.

The initial work-up included a cervical biopsy for establishing histopathological whereby n=52 Squamous cell Carcinoma & n=8 Adenocarcinoma diagnosed. Computed tomography scan (CT) in all patients, additional imaging as Positron emission tomography (PET) was done as per clinical requirement and affordability by the patient. Standard EBRT (Tele Cobalt 60, Make 2009, Model Equinox & Theratron 780 E) to the pelvis followed orthogonal HDR intracavitary brachytherapy (18 Channel HDR Micros electron Iridium 192 Radioisotope ) and a total EQD2 (equivalent dose) of 78.29 Gray was delivered to 69 patients with std. deviation of  $\pm 2.08$  Gray . The treatment outcomes were studied at 36 months post treatment by documenting overall survival & Local pelvic control rate were calculated from the date of completion of treatment CRT & failures were categorized as local pelvic recurrence (cervix, vagina or pelvic nodes) or distant metastases to lymph nodes, bones, or viscera according to the Radiation Therapy Oncology Group criteria.

## Abdominal and Pelvic CT Scans

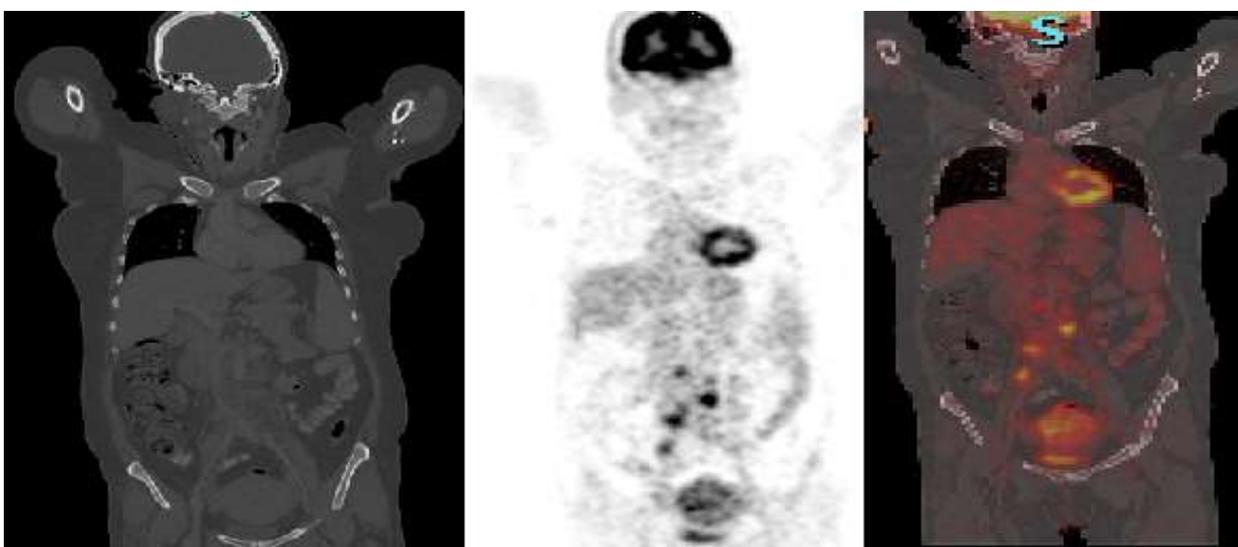
64 Patients had a conventional pretreatment CT scan of the abdomen and pelvis & 32 patients had undergone post treatment CT scan for treatment response evaluation at an in-house facility. These were performed using local imaging protocols and were reported by the center radiologists according to the standard of care and Hounsfield units (HU) were suggested in pretreatment CT Scans only. Post treatment

CT scans were only advised after local examination on 1<sup>st</sup> follow up or thereafter on suspicion of a progressive disease.

## Examination with PET-CT Imaging

The PET-CT examination was performed per institutional protocols. Blood glucose level was required to be less than 100 mg/dL. Whole body images were acquired in 3 D mode 60 minute after intravenous administration 370 MBq (10mCi) of F18 fludeoxyglucose, Oral contrast administered prior to the scan. A low-dose CT used for attenuation correction preceded PET acquisition, and a whole-body PET-CT scan in supine position was obtained from the skull base to the upper thighs. Post Treatment PET CT were advised only 3 months after completion of CRT.[3]

The PET-CT image was interpreted by the nuclear medicine physician at the study site as inhouse facility was not available, Standard Uptake Values (SUV) units were suggested in pretreatment CT Scans only (1). Interpretation of lymph node metastases was based on visual criteria. Specifically, lymph nodes 1 cm in diameter were considered positive if there was fludeoxyglucose uptake greater than that of the surrounding background, and lymph nodes larger than 1 cm in diameter were considered positive.[4]



A

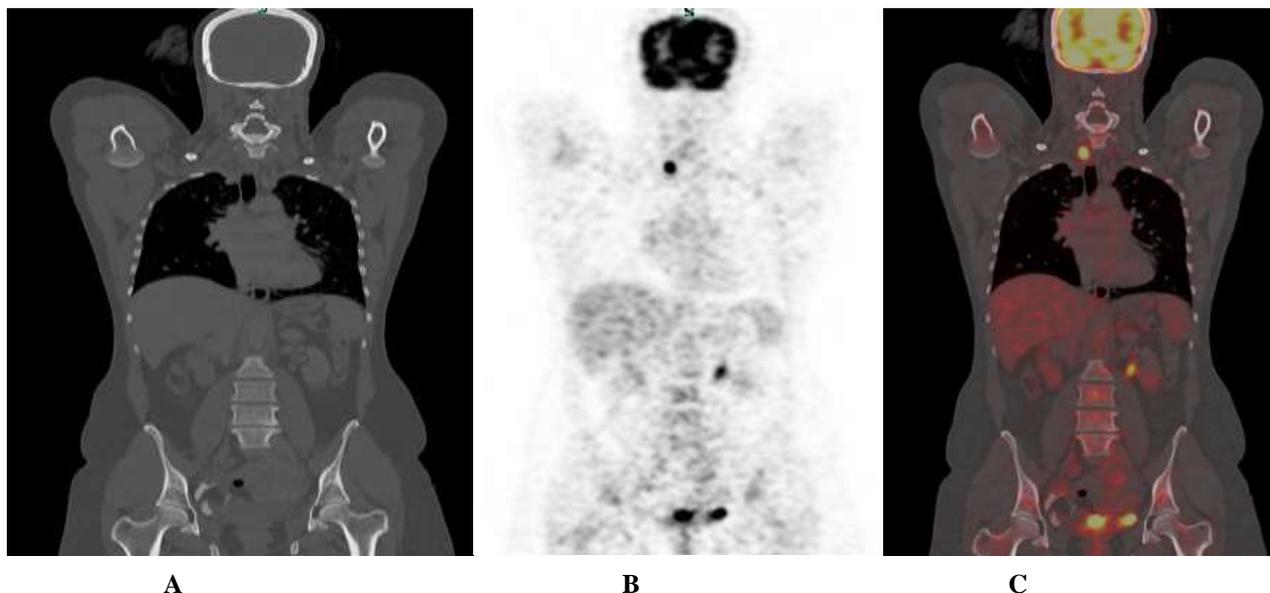
B

C

**Pretreatment CT (A) ,PET (B) & PET CT (C) Scan with Local Disease and abdominal lymphadenopathy**

## Follow-up

On completion of treatment, the patient was seen every 2 months clinically on OPD bases for 1 years & then every 4 months for next year and then every 6 months.[5 &6]



**Post Treatment (A) CT ,PET (B)& PET CT (C)Scan showing Cervical Lymphadenopathy SUV max 8.5 but is not appreciable on CT scan with H U Value 63.**

## Statistical Analysis

A prospective randomized trial with a sample size of 69 patients, 18 Pretreatment PET-CT & 21 post treatment PET CT and 64 Pretreatment CT abdomen-pelvis & 32 Posttreatment CT were done. The association between two categorical variables was evaluated by Chi-Square ( $\chi^2$ ) test. Student's t-test was used to compare continuous variables between the groups. A p-value of less than 0.05 was considered as statistical significance for Chi-Square ( $\chi^2$ ) test and student's t-test. Local control & survival rates were calculated by the Kaplan Meier method. A p-value of less than 0.05 was considered to indicate statistical significance.

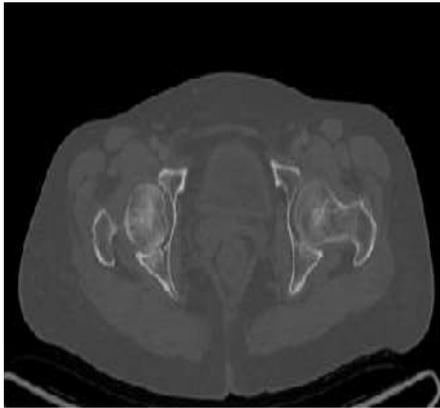
## Results

69 patients were enrolled for participation during April 2017 and June 2020 but slower-than-expected accrual, the trial was stopped in June 2020. 53 patients of 64 CT scan patients survived but 11 patient died & 14 patients reported residual disease locally on CT scan post CRT.

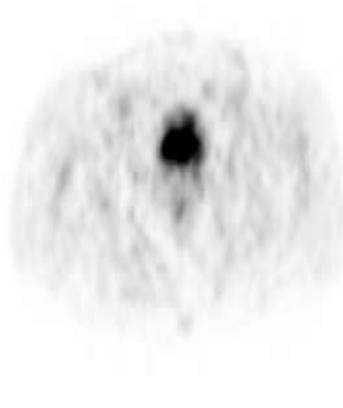
39 PET CT patients N=21 were post treatment & n=18 were pretreatment PET CT & only 3 patients reported residual disease locally on PET CT Scan post CRT and 11 patients had metastasized to different body parts post-treatment. PET findings correlate more highly with outcome than post-treatment CT scan. Despite mild hyper metabolism associated with post-treatment inflammation, PET/CT continues to be highly predictive of LR and OS.

## Primary Outcome

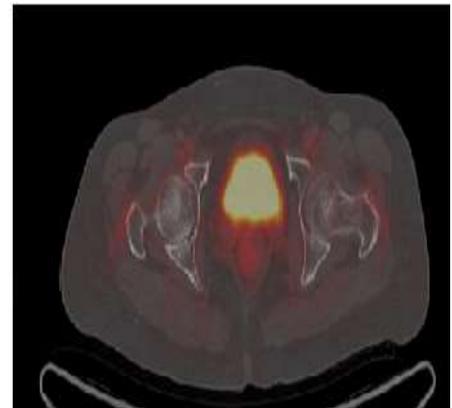
21 patients in the PET-CT group (55.17%) had normal scan results. In the remaining patients, 5 (17.24%) had died though only three patients had residual disease and two of them still survives. Of the 32 patients for whom diagnostic CT results were available, 20 patients (62.5%) had normal scan results, 12 patients (37.5%) had died.



**A**



**B**



**C**

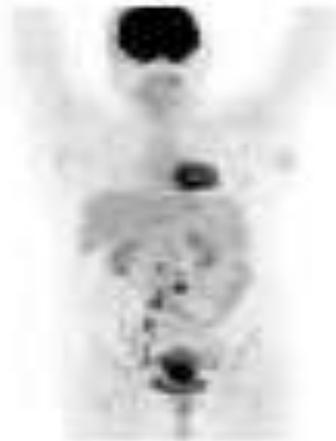
**Post CRT CT (A), PET (B) & PET CT (C) showing complete response to treatment locally.**

#### **Diagnostic CT, PET & PET CT**

An exploratory analysis was conducted to examine a potential association between the presence of pelvic nodes on the diagnostic CT result and the result of the subsequent PET-CT. Twelve of 36 patients (33.3%) with abnormal pelvic nodes on CT had positive para-aortic nodes on PET-CT. In contrast, 8 of 65 patients (12.3%) with normal pelvic nodes on CT had a positive para-aortic node.



**A**



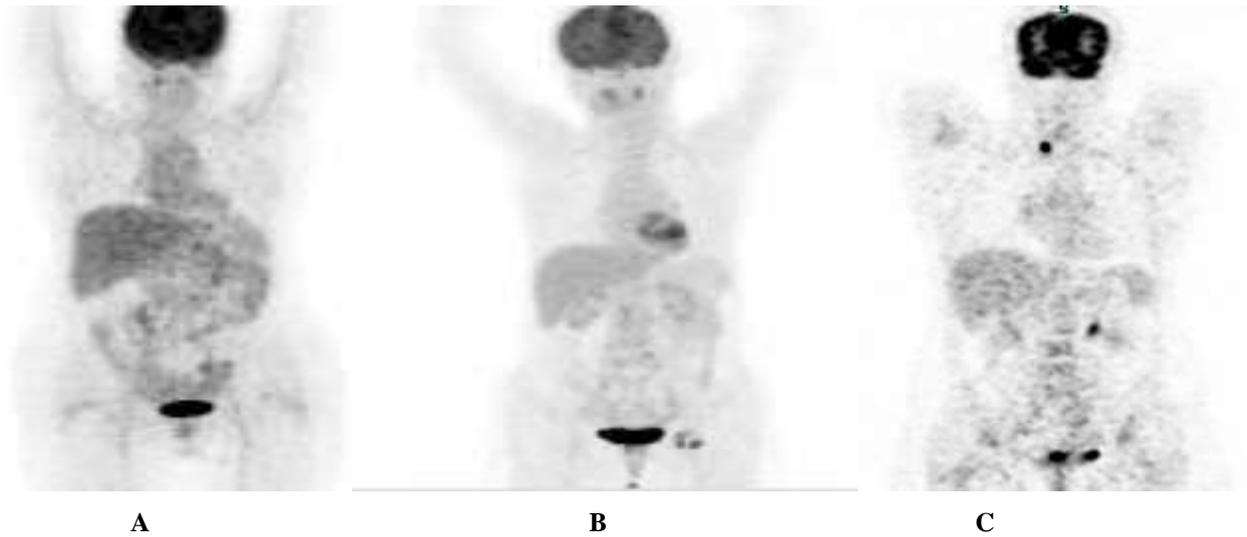
**B**



**C**

**Pre Treatment Diagnostic CT (A), PET (B) & PET CT(C) showing local disease with abdominal Lymph node**

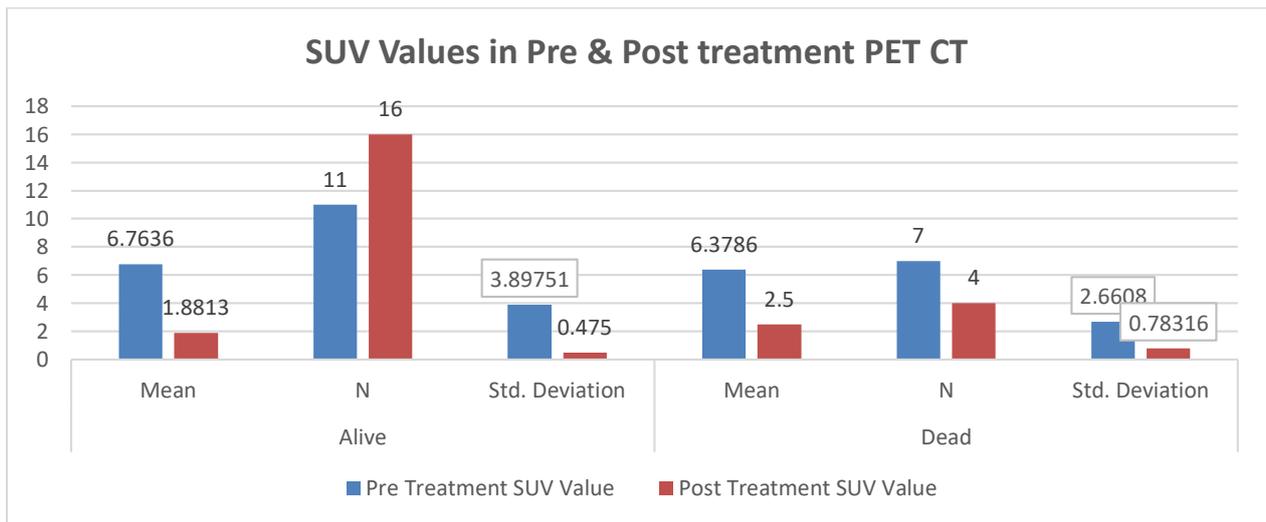
#### **Secondary Outcomes**



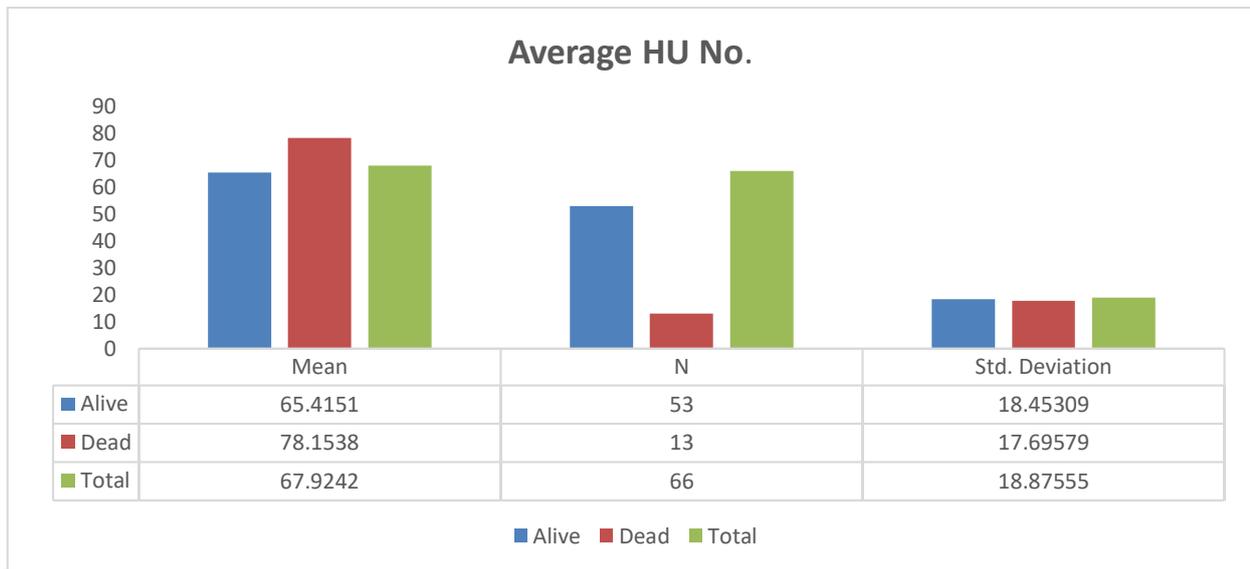
Post CRT MIP image of a (A) complete response,(B) complete local response but metastatic left common iliac lymph node (C) Residual disease locally with cervical lymphadenopathy.

After a median follow-up of 3 years, 21 patients who underwent PET-CT imaging only 3 experienced local recurrence 11 had shown progression compared with 13 patients in with CT alone.

18 patients in the pretreatment PET-CT group who had a mean SUV 6.61 reported SD of  $\pm 3.38$ . & 21 patients in the post treatment PET-CT group who had a mean SUV 2.00 reported with a mean (SD) of .58.

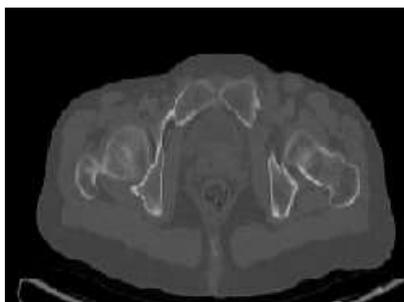


64 patients in the pretreatment CT scan group had a mean Hounsfield no. 67.92 reported SD of  $\pm 18.87$ . & 32 patients in the post treatment CT scan Hounsfield value were not reported by the radiologist.



### Discussion

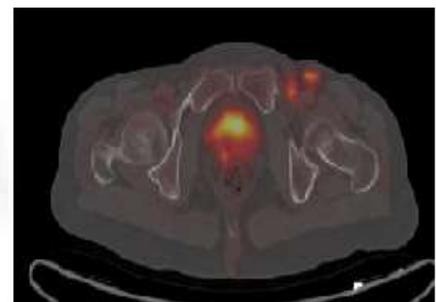
PET-CT could detect more distant metastases than usual CT, resulting in the avoidance of curative CRT, and the detection of more retroperitoneal disease would lead to more extensive radiotherapy. The detection of distant metastatic disease was relatively low, and no significant difference was detected between groups in treatment with radical intent. Though it appeared to be supported as there was an increased rate of detection of para-aortic or common iliac adenopathy identified with PET-CT. although this difference was not statistically significant, likely as a result of the small sample size. There was an increased rate of detection of para-aortic or common iliac adenopathy identified with PET-CT, a pretreatment PET CT was absolutely directive of the intent of curative or palliative treatment in C Cervix. Post treatment PET CT rules out local failure or recurrence as well as distant metastasis that demands PET CT in-house facility a mandatory Imaging modality for a Radiation oncology Department.



**A**



**B**



**C**

**CT (A),PET (B) & PET CT (C) Showing metastatic left common iliac lymph node SUV max. 5.0.**

### Limitations

The trial was stopped prematurely as a result of slow rate of recruitment. The reason not having PETCT facility in-house and Patients had to travel outside the state for the same and the cost PET CT was too high. It was unlikely that patients were able to have a PET-CT outside of the trial, as the government aided health care system would not cover the cost.

In the Himachal Pradesh PET-CT is yet to be adopted for staging of LACC but evaluating the accuracy of the test in detecting lymph nodes and distant metastasis is paramount. Though in other countries, PET-CT for the staging of LACC has not been widely adopted but preferred for the initial workup of stage II to IV cervical cancer. Although the trial was underpowered, it is reasonable to consider the results within the context of the higher-quality evidence to support current practice & finally, a prudent and efficient approach might be to consider PET-CT only when an in-house facility is available within the institutional premises.

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