



## A Prospective Study To Compare T2 Weighted Mri To Ct Imaging In Volume Delineation For Radiotherapy Planning In Carcinoma Cervix

Dr. Lavanya Gopinath<sup>1\*</sup>, Dr. Hemalatha<sup>2</sup>, Dr. Anitha Gopal<sup>3</sup>

<sup>1</sup>Internship Student, <sup>2</sup>Professor, <sup>3</sup>Senior Consultant,

Bangalore Medical College & Research Institute, Bangalore, Karnataka, India

<sup>2</sup>Department Of Obstetrics And Gynecology,

<sup>1,2</sup>Bangalore Medical College & Research Institute, Bangalore, Karnataka, India

<sup>3</sup>Division of Radiation Oncology, Apollo Hospitals, Bannerghatta Road, Bangalore, Karnataka, India

**\*Corresponding Author:**

**Dr. Lavanya Gopinath**

Internship Student, Bangalore Medical College & Research Institute, Bangalore, Karnataka, India

Type of Publication: Original Research Paper

Conflicts of Interest: Nil

### Abstract

**Background:** Cervical cancer is a major health problem in developing countries like India. Appropriate evaluation of disease extent and staging is important as this has an impact on the management, prognosis, and outcome.

**Aim Of The Study** To compare magnetic resonance imaging (MRI), computed tomography (CT), and clinical examination to evaluate the impact of MRI on target volume delineation as compared to the volumes obtained on a CT scan and also to see the effect on staging and prognosis

**Methods:** This prospective study was conducted at Bangalore Medical College in collaboration with Apollo Hospitals, Bannerghatta Road, Bangalore, Karnataka, India, between February 2021 to January 2022. Twenty patients diagnosed with locally advanced carcinoma cervix underwent planning CT abdomen and pelvis which was fused with T2 weighted MRI images to evaluate the impact of MRI on target volume delineation, to see if CT scan along with clinical findings can be a good alternative to MRI scan.

**Results:** MRI was better in tumor delineation as compared to CT scan. Additional imaging gave information regarding the local extent of the disease and nodal involvement. Upstaging of the disease helped in selecting the appropriate treatment modality

**Conclusion:** Result in more accurate radiotherapy treatment planning and also provide prognostic information that would impact the outcome of treatment and survival. CT with good clinical examination could be used as an alternative to MRI where MRI is not feasible.

**Keywords:** MRI, CT, carcinoma cervix, staging, and Radiotherapy planning

### Introduction

Cervical cancer is a major health problem in developing countries like India. Appropriate evaluation of disease extent and staging is important as this has an impact on the management, prognosis, and outcome. The International Federation of Gynecology and Obstetrics is the most commonly used staging system for carcinoma cervix. Since the staging system should be uniform and feasible at all

centers and also allow for comparison of results from different centers,<sup>1</sup> FIGO has recommended staging to be based on clinical findings which include assessment of the tumor extent (ie, the extent of local disease, tumor size, involvement of cervix, vagina, parametrium, and extent into adjacent normal tissue like rectum and bladder) along with limited radiological investigations which do not include MRI

and CT scans for staging in carcinoma cervix.<sup>2</sup> Clinical stagings may be adequate for evaluating local disease extent, but does not take in to account the involvement of the uterus, lymph nodes or distant metastasis. It has been reported in the literature that MRI is superior to CT scan and clinical examination for assessing the tumor and involvement of the uterine body. As patients with carcinoma cervix belong to the lower socioeconomic strata where MRI/CT is not feasible and also as MRI/CT may not be available in all centers it is not possible to do these routinely for staging and management. Hence evaluation in the form of less expensive imaging and thorough clinical examination would be a good alternative that could be carried out.<sup>3</sup> Though the findings on CT, MRI, or PET examinations are not mandatory for FIGO staging could be of additional benefit and provide extra information that would result in stage migration, help appropriate selection of treatment modality (operability, chemotherapy & radiotherapy), and will result in more accurate radiotherapy treatment planning and also provide prognostic information that would impact on the outcome of treatment and survival. Prognostic factors like the stage at presentation, tumor diameter, tumor volume, lymph node metastasis, lymphatic vascular space invasion, deep stromal invasion, microscopic evidence of parametrial invasion, cell type, and hemoglobin level, have an impact on survival.<sup>4</sup> Therefore the revised FIGO staging 2009 has included imaging with MRI in addition to clinical staging where resources permit. In patients with carcinoma cervix, a CT scan is primarily used to evaluate the size of the tumor to detect enlarged lymph nodes, obstruction of the ureter, and any distant metastases to the lung or liver. MRI has better soft tissue contrast resolution than CT scans and has the capability of acquiring images in multi-planar dimensions. It is useful in determining the size of the tumor and in detecting parametrial invasion, bladder, and rectal invasion.<sup>5</sup> It also helps in assessing the presence of enlarged lymph nodes, and obstruction of the ureter, and to detect lung or liver metastases. The conventional two-radiation therapy technique has some shortcomings. Many studies have shown inadequate coverage and the chance of geographical miss in conventional methods when this was assessed with cross-sectional imaging modalities like

computed tomography (CT) or magnetic resonance imaging (MRI).<sup>6</sup>

**Methods:** This prospective study was conducted at Bangalore Medical College in collaboration with Apollo Hospitals, Bannerghatta Road, Bangalore, Karnataka, India, between February 2021 to January 2022. Twenty patients diagnosed with locally advanced carcinoma cervix underwent planning CT abdomen and pelvis which was fused with T2 weighted MRI images to evaluate the impact of MRI on target volume delineation, to see if CT scan along with clinical findings can be a good alternative to MRI scan. During this period, 20 women with locally advanced biopsy-proven squamous cell carcinoma cervix underwent, T2-weighted MRI in addition to planning CT scan were enrolled in this study. Approval from the institutional research and ethics committee was obtained. All suitable subjects were explained about the study and were provided with informed consent with details of the study. After reading it and the clarification of any doubts, they were enrolled in the study after obtaining their written informed consent. Inclusion criteria: Female patients of more than 18 years of age, Diagnosed to have squamous cell carcinoma cervix IIA- IIB [FIGO staging], Being planned for treatment with radical chemo-irradiation, ECOG 0-1, Willing to participate in the trial. Exclusion criteria: previous irradiation to the pelvis, another malignant disease. All patients underwent treatment simulation, before initiation of radiotherapy. Patients either underwent conventional radiotherapy planning with conventional technique or conformal radiotherapy technique (3DCRT, IMRT). Immobilization with Vacloc was done in patients who were undergoing conformal radiotherapy. Patients are simulated supine with arms on the chest, knees, and lower legs immobilized, and anterior and lateral tattoos marked with radio-opaque material, aligned with lasers to prevent lateral rotation. Planning CT scans were taken from the level of the diaphragm to 5 cm beyond the vaginal introitus. Imaging was performed in these 20 patients to assess tumor size, locoregional extent, and pelvic nodal status and these images were used for radiotherapy planning. Intravenous contrast is used to outline pelvic blood vessels to be used pelvic nodes in CTV delineation. It may also enhance the GTV primary. Oral contrast was given to all patients to outline the bowel. MRI scans were performed on a

3-T MR scanner (Intera Achieva) according to the Radiology department protocol for pelvic malignancies, Axial T2 weighted HR images were primarily assessed. Imaging parameters for the T2W HR images are given below. Repetition time (TR) 3625 ms, echo time (TE)100 ms, echo train length 12, bandwidth 21.78kHz, field of view 32 cm, slice thickness 3 mm, gap 0mm, number of excitations 3, no phase wrap, matrix 352x293. The investigational imaging MRI was compared with CT imaging to compare the target volume delineation and evaluate the impact of MRI on target volume as compared to the volumes obtained on a CT scan in terms of assessment of GTV Primary (Cervical tumor, involvement of uterus, vagina, and parametrium) and GTV Lymph nodes. The study also looked at any change in the staging of the disease based on additional information from image modalities which will change the management and prognosis in these patients. The attempt was made to see if a CT scan along with clinical findings can be a good alternative to an MRI scan. Another objective was to look at the possibility of a reduction in treatment volume based on MRI when compared to CT-based planning. Evaluation was also done to check the possibility of avoiding invasive procedures like cystoscopy based on MRI/CT findings.

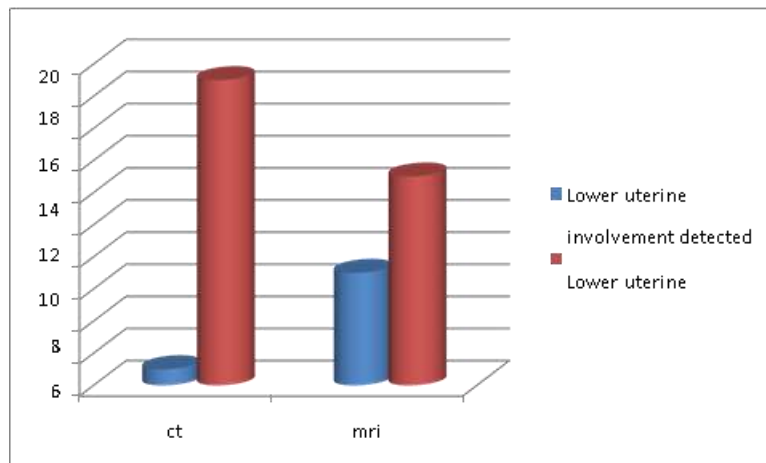
### Statistical Analysis

A descriptive analysis and frequency distribution of the patient characteristics was done. Fisher's Exact test was done to find out the relationship between prognostic factors and image findings. PABAK was done to compare different imaging modalities (CT versus MRI). Paired T-test was used for tumor volume comparison.

### Results

Twenty patients, diagnosed with locally advanced carcinoma cervix underwent planning CT scan of abdomen pelvis and T2 Weighted MRI pelvis. Data were collected and analyzed. Most of the patients belonged to the age group between 40 to 50 years (12 out of 20 patients). Among them, 2 patients were below the age of 40 and 4 patients were in the age group of 50 to 60 years and 2 patients were above 60 years. The main presenting complaint was white discharge per vaginum (13 out of 20 patients ) bleeding per vaginum (11 out of 20 patients ) and low backache (10 out of 20 patients ) Among 20 patients, 15 were clinically staged as FIGO stage IIIB and patients belonged to FIGO stage IIB. Primary tumor assessment was done by clinical examination and different modalities of imaging like ultrasonography, CT abdomen pelvis, and MRI pelvis.

**Graph :1 Lower uterine segment involvement assessment**



Graph 1 shows MRI showed lower uterine segment involvement in 6 out of 20 patients and CT scan showed uterine involvement in only one patient

**Graph:2 Assessment Of Parametrial Extension**

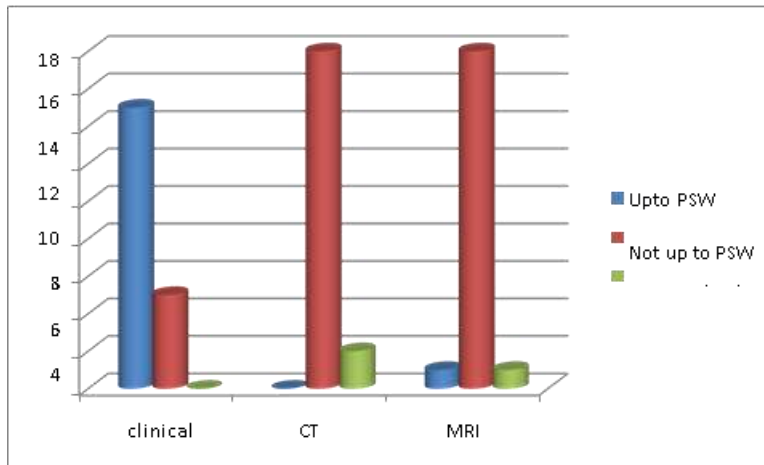
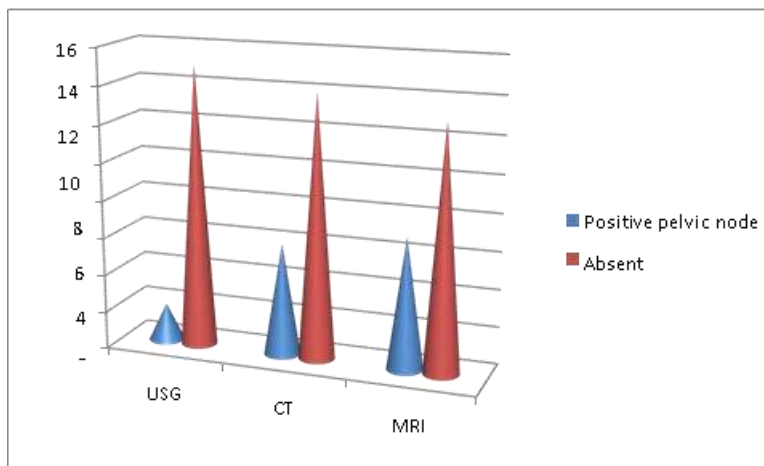


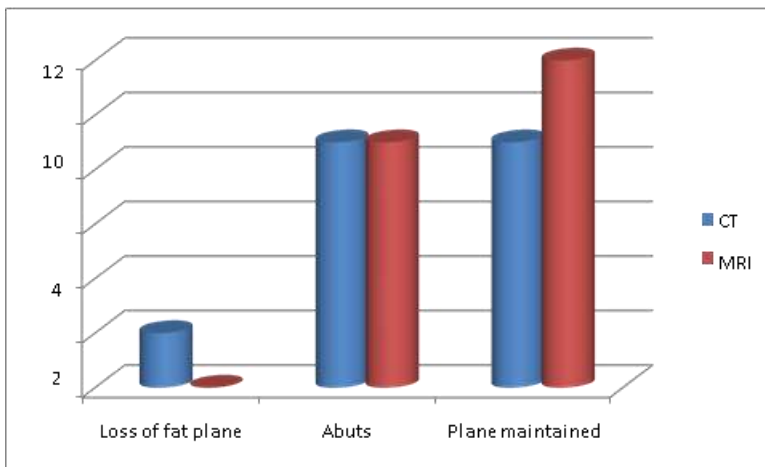
Table All 20 patients showed parametrial involvement on clinical examination, while MRI showed involvement in 18 patients. Clinically parametrial involvement was up to the pelvic sidewall in 15 out of 20 patients while this was seen only in 1 patient on MRI. For the remaining 14 patients with clinical 3B disease, there was bulky parametrial disease on MRI but this was not the up to pelvic sidewall. CT scan showed parametrial involvement in 18 of the 20 patients, not extending up to the pelvic side wall, but it was difficult to make out the extent of parametrial involvement on CT scan.

**Graph :3 Assessment of pelvic lymphadenopathy**



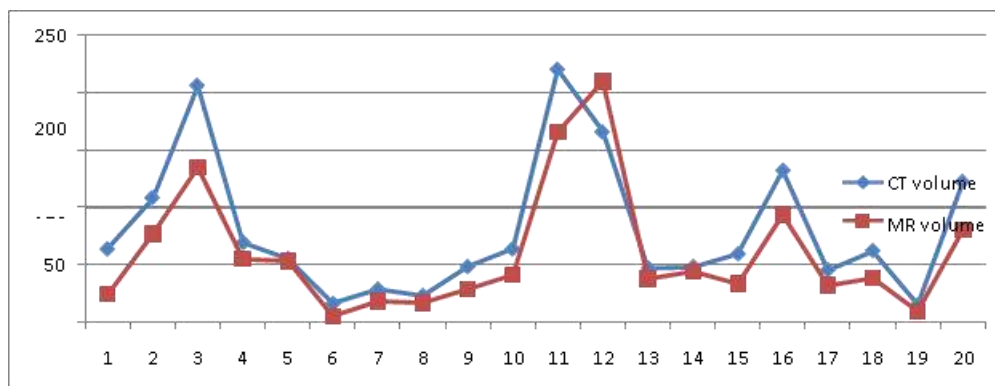
Graph :3 Detection of pelvic lymphadenopathy was assessed by these imaging modalities and a comparison was done between USG abdomen, CT, and MRI done in only 17 patients as only 17 patients had undergone USG abdomen in our study. The comparison was done between CT, abdomen, and MRI pelvis in detecting pelvic nodes in 20 patients. CT and MRI had similar findings and Ultrasonography estimated pelvic lymphadenopathy.

**Graph:4 In assessing bladder involvement**



Graph:4 CT scan showed loss of fat plane with the bladder in 2 patients and one of these patients had a tumor abutting the bladder on MRI. Tumor abutting bladder was seen in 6 patients on both CT scan and MRI, 3 patients on CT scan only, and 2 others on MRI only. Cystoscopy was normal in all these patients. There were 2 patients, one with bladder mucosal irregularity and another one with trigonal edema on cystoscopy, the biopsy from the lesion was negative for malignancy. Imaging did not pick up these 2 changes. The patient with bladder mucosal irregularity had findings of tumor abutting bladder on MRI but normal findings on CT.

**Graph:5 Target volume delineation based on CT and MRI**



**Table 1 Volume of cervical growth based on CT and MRI**

	<u>Mean volume</u>
Tumor volume on CT scan	79.8
Tumor volume on MRI scan	59.7
Difference	20.02



Table 1 & Graph:5 Mean volume of primary growth measured by CT scan was 79.8 cm<sup>3</sup> and MRI was 59.7 cm<sup>3</sup> with a difference of 20.02 cm<sup>3</sup>, which was statistically significant by Paired t-test. The posterior extent of the primary lesion was up to the level of S2 and beyond in a total of 18 patients with 11 patients having tumors up to the level of S2, 6 patients up to the level of S3 and 1 patient beyond S3. The position of the uterus was retroverted in one patient and was beyond the posterior border of the conventional four-field box technique which was kept at the S2/S3 junction. Therefore the conventional field would have resulted in gross tumour being beyond the target volume in 12 patients, having inadequate tumour volume margin in 7 patients and therefore would have been inadequate in 19 out of 20 patients. It was found that disease progression in 6 out of 9 patients, who had anteroposterior (AP) tumor diameter of more than 4 cm. There was only 1 patient, who had disease progression out of 8 patients, with an AP diameter less than 4 cm. Statistical analysis with Fisher's exact- showed significant p-value (0.05). This showed a significant association between anteroposterior diameter > 4cm with disease progression. Significance of tumor volume more than 50 mm<sup>3</sup> and disease progression In 6 out of 12 patients with tumor volume more than 50 cm<sup>3</sup> had disease progression, compared to only one out of 5 patients with tumor diameter less than 50 cm<sup>3</sup> had disease progression. This Appears to be significant but was not statistically significant due to less number of patients. Relationship between tumor volume and nodal status. 8 out of 15 patients with tumor volume, more than 50 cm<sup>3</sup> had pelvic lymphadenopathy, compared to only one out of 5 patients with a tumor diameter less than 50 cm<sup>3</sup>. This Appears to be significant but was not statistically significant due to less number of patients.

## Discussion

Uterine cervical neoplasm is a major health problem in developing countries like India. Appropriate evaluation of disease extent and staging is important as this has an impact on the management, prognosis, and outcome.<sup>7</sup> The International Federation of Gynecology and Obstetrics is the most commonly used staging system for carcinoma cervix. Since the staging system should be uniform and feasible at all centers and also allow for comparison of results from different centers, FIGO has recommended staging to

be based on clinical findings which include assessment of the tumor extent (ie, the extent of local disease, tumor size, involvement of cervix, vagina, parametrium, and extent into adjacent normal tissue like rectum and bladder) along with limited radiological investigations which do not include MRI and CT scans for staging in carcinoma cervix. Clinical staging may be adequate for evaluating local disease extent but does not take into account the involvement of the uterus, lymph nodes, or distant metastasis. It has been reported in the literature that MRI is superior to CT scan and clinical examination for assessing the tumor size and involvement of the uterine body. All patients with carcinoma cervix should be jointly evaluated with detailed history and physical examination by the Radiation and Gynecologic oncologist.<sup>8</sup> Examination under anesthesia provides a better assessment of primary tumor in early-stage disease. In all patients with stage IIB and more advanced disease and in those patients who have a history of urinary or lower gastrointestinal tract complaints, cystoscopy or rigid recto sigmoidoscopy is recommended to rule out local infiltration. In cervical cancer, a tumor is visualized as a soft tissue mass on CT imaging, which often results in enlargement of the cervix. Generally, there will be non-homogenous enhancement around the tumor following contrast administration with areas of necrosis and ulceration seen as hypodense areas within it. Evidence of parametrial soft tissue mass, any irregularity of the lateral margins of the cervix, and obliteration of periureteral fat planes are indicators that suggest parametrial invasion, but these are not definitive indicators. Therefore it is difficult to make out parametrial infiltration on CT imaging.<sup>9</sup> Creasman WT et.al (ACRIN6651 /GOG intergroup study), in their study comparing MRI, CT, and clinical examination for delineating early cervical cancer, reported that MRI was superior to CT and clinical examination in assessing tumor size.<sup>10</sup> In a prospective study by Eifel PJ, et al, which included 208 women, most with stage IB diseases underwent pretreatment MRI and CT It was found that MRI correlated more closely with surgicopathologic findings than CT or physical examination. This study also showed that there was an overestimation of tumor size in both imaging modalities.<sup>11</sup> All 20 patients showed parametrial involvement on clinical

examination, while MRI showed involvement in 18 patients. Clinically parametrial involvement was up to the pelvic side wall in 15 out of 20 patients while this was seen only in 1 patient on MRI. For the remaining 14 patients with clinical 3B disease, there was bulky parametrial disease on MRI but this was not up to pelvic sidewall. CT scan showed parametrial involvement in 18 of the 20 patients, not extending up to the pelvic side wall, but it was difficult to make out the extent of parametrial involvement on CT scan. Therefore in our study, the local tumor extent into parametrium was more on clinical assessment than what was detected on both imaging modalities. Between CT and MRI findings, the tumor was better seen on MRI and the findings correlated better with clinical findings than CT scan.<sup>12</sup> Fuller AF, et.al in their study among 23 patients, pretreatment evaluation with MRI reported a sensitivity of 87.0% and a specificity of 79.0% with 3 false negative reports for detecting vaginal involvement.<sup>13</sup> In a study by Nahhas WA, et.al the efficacy of MRI in detecting lower uterine segment involvement was found to be superior with a specificity of 99.0%. In our study, MRI was found superior to CT in detecting lower uterine involvement. MRI showed lower uterine segment involvement in 6 out of 20 patients and CT scan showed uterine involvement in only 1 patient. Detection of lower uterine segment involvement is important as this is associated with a bad prognosis and this cannot be made out on clinical examination. Multiple studies have shown that the accuracy of CT scans in staging cervical cancer ranges from 63% to 88%.<sup>(27)</sup><sup>14</sup> In the detection of lymph nodes the accuracy is found to be 77% to 85%. y of 93%<sup>(28)</sup>. In his study, Boyce JG, et al. compared pretreatment examination under anesthesia (EUA), transrectal ultrasonography (TRUS), and MRI in assessing tumor volume and staging in 60 patients with invasive carcinoma of the cervix. It was found that MRI was superior in assessing the tumor extent and lymph node enlargement when compared to TRUS and EUA.<sup>15</sup> The tumor was better seen and it was easy to delineate on MRI. Most of the time, it was difficult to make out tumors from surrounding normal cervical stroma with a CT scan and therefore could have been overestimated. 3D Conformal radiotherapy uses a set of fixed radiation beams that are shaped using the projection of target volume and have a uniform intensity across the field. The use of

intensity-modulated radiotherapy confines the high-dose portions of the radiation field to nontraditional shapes. IMRT has been shown to reduce normal tissue irradiation and has been associated with reduced acute and chronic toxicity compared with 3DCRT.<sup>16</sup> Accurate delineation of GTV and CTV is an important advantage of image-based planning. Thus addition of MRI is likely to give a better and accurate tumor volume delineation which would in turn translate into an appropriate dose to the tumor with more sparing of the normal tissues.<sup>17</sup> Posterior extent of the primary lesion and change in conventional field borders based on imaging findings.<sup>18</sup> The commonly used field borders for the lateral fields were the anterior aspect of the symphysis and the S2/S3 interspace.<sup>19</sup> Ports defined by these guidelines will not always be suitable for patients presenting with different stages and local extent of disease. Based on intra-operative measurements, Hacker NF. et al opined that the entire anterior sacral silhouette should be included in the lateral field in patients with locally advanced carcinoma cervix, due to the posterior extension of the tumor.<sup>20</sup>

## Conclusions

This pilot project done to compare T2 W MRI to CT imaging in volume delineation for radiotherapy planning in carcinoma cervix showed that imaging modalities have a role in accurate delineation of gross tumor volume (GTV). Though the findings on CT, MRI, or PET examinations are not mandatory for FIGO staging they could be of additional benefit and provide extra information that would result in stage migration, help appropriate selection of treatment modality, result in more accurate radiotherapy treatment planning and also provide prognostic information that would impact on the outcome of treatment and survival. Image-based planning would in turn translate into an appropriate dose for the tumor with more sparing of the normal tissues. It would also reduce geographical miss during treatment planning. MRI appears to be better than CT for locoregional disease assessment, especially for primary tumor and adjacent soft tissue extension. CT with good clinical examination could be used as an alternative to MRI where MRI is not feasible. Bowel and bladder preparation is required before CT and MRI for better fusion with more accurate delineation of the target and OAR.

## References

1. Eifel PJ, Morris M, Wharton JT, Oswald MJ. The influence of tumor size and morphology on the outcome of patients with FIGO Stage IB squamous cell carcinoma of the uterine cervix. *Int J Radiat Oncol Biol Phys.* 1994;29:9–16.
2. Kupets R, Covens A. Is the International Federation of Gynecology and Obstetrics staging system for cervical carcinoma able to predict survival in patients with cervical carcinoma? An assessment of clinimetric properties. *Cancer* 2001; 92: 796–804
3. Downey GO, Potish RA, Adcock LL, Prem KA, Twiggs LB. Pretreatment surgical staging in cervical carcinoma: therapeutic efficacy of pelvic lymph node resection. *Am J Obstet Gynecol* 1989; 160: 1055–1061
4. Van Nagell JR, Breenwell N, Powell DF, et al. Microinvasive carcinoma of the cervix. *Am J Obstet Gynecol.* 1983;145:981–989.
5. Hasumi K, Sakamoto A, Sugano H. Micro invasive carcinoma of the uterine cervix. *Cancer.* 1980;45:928–931.
7. Simon NL, Gore H, Shingleton HM, et al. Study of superficially invasive carcinoma of the cervix. *Am J Obstet Gynecol.* 1983;145:981–991.
8. Maiman MA, Fruchter RG, Di Maio TM, Boyce JG. Superficially invasive squamous cell carcinoma of the cervix. *Obstet Gynecol.* 1988;72:399–403.
9. Buckley SL, Tritz DM, van Le L, et al. Lymph node metastases and prognosis in patients with Stage IA2 cervical cancer. *Gynecol Oncol.* 1996;63:4–9.
10. Creasman WT, Zaino RJ, Major FJ, et al. Early invasive carcinoma of the cervix (3 to 5 mm invasion): risk factors and prognosis. A Gynecologic Oncology Group study. *Am J Obstet Gynecol.* 1998;178:62–65.
11. Eifel PJ, Berek JS, Thigpen JT. Cancer of the cervix, vagina, and vulva. In: DeVita VT, Hellman S, Rosenberg SA, editors. *Cancer: Principles and practice of oncology.* Philadelphia: Lippincott Williams & Wilkins, 1997:1433–1478.
12. Chung CK, Nahhas WA, Stryker JA, Curry SL, Mortel R. Analysis of factors contributing to treatment failures in Stages IB and IIA carcinoma of the cervix. *Am J Obstet Gynecol.* 1980;138:550–556.
13. Fuller AF, Elliott N, Kosloff C, Lewis JL. Lymph node metastases from carcinoma of the cervix, Stages IF and IIA: implications for prognosis and treatment. *Gynecol Oncol.* 1982; 13:165–174.
14. Nahhas WA, Sharkey FE, Whitney CW, et al. The prognostic significance of vascular channel involvement and deep stromal penetration in early cervical carcinoma. *Am J Clin Oncol.* 1983;6:259–264.
15. Boyce JG, Fruchter RG, Nicastrì AD, et al. Vascular invasion in Stage I carcinoma of the cervix. *Cancer.* 1984;53:1175–1180.
16. Burke TW, Hoskins WF, Heller PB, Bibro MC, Weiser EB, Park RC. Prognostic factors associated with radical hysterectomy failure. *Gynecol Oncol.* 1987;26:153–159.
17. Delgado G, Bundy B, Zaino R, et al. Prospective surgical pathological study of disease-free interval in patients with Stage IB squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. *Gynecol Oncol.* 1990;38:352–357.
18. Kamura T, Tsukamoto N, Tsuruchi N, et al. Multivariate analysis of the histopathologic prognostic factors of cervical cancer in patients undergoing radical hysterectomy. *Cancer*
19. De Gaetano AM, Vecchioli A, Minordi M, et al. Role of diagnostic imaging in abdominal lymphadenopathy. *Rays.* 2000;25:463–484.
20. Hacker NF. Cervical cancer. In: Berek JS, Hacker NF. *Practical gynecologic oncology*, 3rd edition. Philadelphia: Lippincott Williams & Wilkins, 2000:345–405.