

# **CLINICAL PRACTICE GUIDELINES**

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**MOH/P/PAK/60.03 (GU)**

## **MANAGEMENT OF CERVICAL CANCER**



**MINISTRY OF HEALTH MALAYSIA**

**ACADEMY OF MEDICINE**

## Statement of Intent

This clinical practice guideline is meant to be a guide for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily ensure the best outcome in every case. Every health care provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

## Review of the Guidelines

This guideline was issued in 2003 and will be reviewed in 2005 or sooner if new evidence becomes available

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All those who had provided valuable input and feedback

The secretariat for their patience, support and services rendered.

## **GUIDELINE DEVELOPMENT AND OBJECTIVES**

### **Guideline Development**

The workgroup comprised obstetricians and gynecologists, oncologists, pathologists and public health specialists. These guidelines are based on the best available current evidence.

### **Objectives**

The main aim of these guidelines is to assist health care providers in clinical decision making by providing well-balanced information on the management of patients with cancer of the cervix. It is also hoped to decrease the incidence of cancer cervix and standardise clinical management.

### **Clinical Question**

The clinical questions of these guidelines are:

- (i) How can cancer cervix be picked up?
- (ii) How can it be treated, and also prevented?

### **Target Population**

These guidelines are developed to apply to women at risk as well as patients with cancer of the cervix

### **Target Group**

These guidelines are meant for all health care providers.

### LEVELS OF EVIDENCE SCALE

I	Evidence obtained from at least one properly randomized control trial
II - 1	Evidence obtained from well-designed controlled trials without randomization
II - 2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group
II - 3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III	Opinion of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees

*SOURCE: U.S./CANADIAN PREVENTIVE SERVICES TASK FORCE*

## **SUMMARY**

Cervical cancer is one of the common genital tracts in woman. Prevention, early diagnosis and treatment has been shown to reduce mortality due to cervical cancer. Cytological screening using the Papanicolou (Pap) smear test remains the most effective strategy for the detection of precancerous state and consequent control of cervical cancer. Most countries which have been able to significantly reduce morbidity and mortality due to this disease has attributed it to effective cervical screening programme and early treatment.

The options for treatment of invasive cervical cancer in general are surgery, radiotherapy and chemotherapy. Treatment for the less common conditions adenocarcinoma of cervical similar to squamous carcinomas especially in early disease. In invasive cervical cancer during pregnancy treatment options are similar to non-pregnant patient. In this situation the patients would be actually involved in decision making as the period of gestation and viability of the fetus are important determinines.

Palliative treatment is the choice of treatment for patients with metastatic disease or with recurrent cancer, in very elderly patients, or those with extreme medical conditions.

Close follow up should be directed to patients with poor prognostic factors, and to detect early recurrence in those for whom potentially curable treatment exists. The ideal frequency of follow up has not been evaluated. However, 3 monthly follow up for the first three years, 6 monthly for the third to fifth year and annually after the fifth year is often recommended.

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## **1. INTRODUCTION**

Cervical cancer is the most common cancer after cancer of breast, in women worldwide with an annual incidence estimated in excess of 440,000 cases. However, in Malaysia it comes after cancer ovary. No other cancer better documents the remarkable effects of prevention, early diagnosis and treatment on the mortality rate than cancer cervix. (Patterson et al, 2001). From the leading cause of cancer mortality in women in United States, cancer cervix dropped markedly to being the 8<sup>th</sup> source of cancer mortality (Cotran et al, 1999). In contrast to its reduced mortality, the detection frequency of early cancer and pre-cancer have increased dramatically (Silverberg et al, 1989). In the United States, annually there are an estimated 13,000 cases of new cancer and 50,000 of advanced pre-cancerous conditions (Silverberg et al, 1989). Over half of invasive carcinomas are cured by early detection and effective therapy and many more pre-cancerous lesions are eradicated by timely and appropriate treatment. In this under score, cytological screening (through Papanicolou (Pap) smear test ) as an effective screening tool for detection of precancerous state and control of cervical cancer. The accessibility of the cervix to colposcopy and biopsy has also assisted in this. Canada has better results –impact of Pap smear.

## **2. SCREENING**

Although the benefits of cervical screening were described over seventy years ago, resource limitations have prevented achieving the benefits of cervical screening worldwide, particularly in developing countries, where prevalence of the disease is high. Organized whole population screening is more effective than opportunistic screening (FIGO Committee on Gynaecological Oncology, 2000).

In Malaysia, Pap smear screening has been available since the 1960s, yet cervical cancer remains the second most common genital cancer afflicting Malaysia women it was the eighth leading cause of death amongst medically certified deaths in 1998 (Kasri., 1993). Nearly eighty percent of patients with cervical cancer presented with advanced disease, stages IIB – IVA3 (Azhar et al, 1989). Based on the Penang Cancer Registry in 1996, the age-standardised incidence rate for cervical cancer was 16.2 per 100,000 population as compared to breast cancer (23.8 per 100,000 population). Despite the availability of cervical cancer screening, 10.5% of female cancer deaths at government hospitals are contributed by cervical cancer (i.e 119 deaths in 1998) whereas 7.9% (2,000-3,000 annually) of all cancer admissions in government hospitals are diagnosed as cervical cancer. Since the launching of the Healthy Life Style Campaign against cancer in 1995, both public and private sectors have contributed to the strengthening of the screening programme, with an increase in Pap smears taken from 97,989 in 1994 to 344,767 in 1996. In 2000, 0.95 % of the 391,983 Pap smears taken were reported positive. In 2001, there were 3,185 (1.1%) out of 202, 550 Pap smear slides reported positive based on the Bethesda Classification System of which 4.9% of the positive smear were reported as carcinoma of the cervix.

## **2.1. Method of Screening**

A variety of devices are available to obtain cervical samples such as the spatula with cytobrush, Accellon Combi cervical biosampler, Papette etc (Figo Committee on Gynaecological Oncology, 2000). The specimen once taken, is generally smeared on a glass slide, wet-fixed in 95% ethanol or cytospray, and sent to the laboratory for staining and screening. Recently, the advent of liquid based cytology has improved the sensitivity of cytologic screening (Austin et al, 1998). Computerized screening devices like Papnet and AutoPap, for primary screening or for rescreening of negative cases, have offered the possibility of greater sensitivity and specificity, albeit with an added cost (Grohs, 1982). The use of HPV typing as a potential primary screening tool is currently under evaluation (Figo Committee on Gynaecological Oncology, 2000).

## **2.2. Frequency of Screening**

It has been seen that women who do not participate in screening programs, and women whose interval between smears is more than 3 years, are at highest risk for developing cervical carcinoma (Figo Committee on Gynaecological Oncology, 2000).

In Malaysia, all women who are, or who have been sexually active, between the ages of 20 and 65 years, are recommended to undergo Pap smear testing. If the first two consecutive Pap results are negative, screening every three years is recommended.

## **3 MANAGEMENT OF ABNORMAL SMEAR**

In Malaysia, standard management of smear-detected abnormalities was adopted during a national consensus meeting in 1997, and this was further amended by a working committee within the National Pap Smear Screening Technical Committee in 2000 (refer Appendix 1).

## **4. TERMINOLOGY AND CLASSIFICATION**

The first classification of cervical smears of the fifties was the Papanicolaou system that devised a numeric system of five classes (0 to V) (Papanicolaou, 1949; Solomon, 1992). This soon gave way to the dysplasia terminology (Reagan et al, 1953), and was replaced by Richart's cervical intraepithelial neoplasia (CIN) terminology in the seventies (Richart, 1973). In December 1988, the National Cancer Institute (NCI) sponsored a workshop to develop a uniform descriptive diagnostic terminology for cervico-vaginal cytology, the Bethesda System (TBS) (Koss, 1990). This provided a comprehensive format for reporting cervico-vaginal cytology (NCI workshop, 1989), and has been adopted by many laboratories worldwide, (Schenk et al, 1998) with or without modification like the Australian modified TBS (Farnsworth, 2001).

In Malaysia, the CIN staging was first adopted for reporting of Pap smears. In 1997, the consensus Meeting on the National Pap Smear Screening Programme agreed to use TBS. In 2001, the request and reporting form (PS 1/98 pindaan) was gazetted to be used by all service providers both public and private (Appendix 2)

## 5 DIAGNOSIS OF INVASIVE CERVICAL CANCER

The diagnosis of micro-invasive cervical cancer should be based on histological examination of removed tissue, preferably a cone that includes the entire lesion of the cervix colposcopic directed biopsy of suspicious lesions is preferred histological confirm of cervical cancer is mandatory.

## 6. INVESTIGATIONS FOR INVASIVE CERVICAL CANCER

Once invasive cervical cancer is diagnosed, the following investigations are recommended:

- Blood tests
  - Full blood count
  - Liver function test
  - Renal profile

At present there are no reliable blood tumour markers for cervical cancer.

- Imaging
  - Intravenous urography (IVU)
  - Chest X-ray

CT scan is desirable especially for stages III and IV, as it may reveal paraortic nodes, as well as the size of the primary tumour. Patients who have had a CT scan need not have an IVU. MRI of the pelvis is preferable, but may not be always practical in our context.

Patients with Hb < 10 gm/dL at any point in time during radiotherapy, should have a packed cells transfusion since the ideal hemoglobin level is > 12 gm/dL.

## 7. TREATMENT OF CERVICAL CANCER

For patients undergoing Examination under anesthesia (EUA), it would be desirable for radio-opaque marker clips to be placed on the cervix as well as the lowest extent of the tumour. The posterior extension of the tumour should also be noted at this point. This would assist in radiotherapy planning.  
The options for treatment of cervical cancer are:

Surgery  
Radiotherapy  
Chemotherapy

Radical surgery is the preferred option in younger women and in sexually active women, as radiotherapy results in significant sexual impairment (Grumann, 2001; Schover, 1989) [Level III]. Surgery should be carried out by gynaecologists with training in radical gynaecological cancer surgery. Apart from this, the availability of clinical oncologists and radiotherapy facilities should also influence the decision.

## **7.1 Surgery**

### **7.1.1 Stage I-A1**

In stage I-A1, the incidence of lymph node involvement is very low (Coppleson; 1992) [Level III]. The prognostic significance of lymphovascular involvement is uncertain. Conisation is appropriate in patients who wish to preserve their fertility, if there is no evidence of lymphovascular space invasion, and the margins of the cone excision are clear. For patients who do not wish to have their fertility preserved, a simple hysterectomy is adequate, with the ovaries being conserved in pre-menopausal patients.

### **7.1.2 Stage I-A2, IB and II-A**

In IA2 disease, the incidence of lymph node metastasis is 4 to 10% (Miller et al, 2000). The lateral parametrial dissection need not be as extensive as in IB and II-A disease. Patients in stage I-A2 can be treated with modified radical hysterectomy and bilateral pelvic lymphadenectomy, or radiotherapy. Those with stage IB and II-A diseases can be treated with radical hysterectomy and bilateral pelvic node dissection (Wertheim's hysterectomy), or primary radiation therapy, with equivalent results. The choice of treatment should be influenced by such factors as ovarian preservation, co-morbid conditions and potential side effects [Level II-1]

If grossly involved pelvic nodes are detected at the time of radical hysterectomy, excision of these nodes has been found to improve local control (Hacker et al, 1995) [Level III].

## **7.2 Radiotherapy**

Radiotherapy may be curative in all stages of cervical cancer and is the treatment of choice for stages IIB – IVA. Early cervical cancer, (Stages I – IIA), may be treated with surgery or radiotherapy with equivalent cure rates although the complication rate may be higher with the latter. (Landoni et al, 1997) [Level I]. When resources for surgery are limited, radiotherapy should be considered. Radiotherapy is indicated for the following affect:

- (i) Primary radical / curative
- (ii) Pre-operative
- (iii) Adjuvant
- (iv) Palliation

Although radiotherapy alone may be curative in cervical cancer, combined chemo-radiotherapy has shown superior cure rates (Whitney et al, 1999; Morris et al, 1999; Keys et al, 1999; Rose et al, 1999; Peters et al, 2000) [Level I]. In general when radical

radiotherapy is considered, concurrent chemo-radiotherapy is the treatment of choice for bulky stage IB diseases, stages II – IVA and

The aim of radiotherapy is to deliver a tumouricidal radiation dose with optimal cure rates and minimal complications.

Radiotherapy is divided into external beam radiotherapy and brachytherapy.

### **7.2.1 External beam radiotherapy (EBRT)**

External beam radiotherapy is used to treat the primary tumour and pelvic nodes. Radiotherapy to the pelvis only is recommended for cervical cancer. Although a large Radiotherapy Oncology Group trial has shown the benefit of prophylactic para-aortic radiotherapy (Rotman et al, 1995) [*Level I*], this has been shown to be inferior to pelvic chemo-radiotherapy (Morris et al, 1999 [*Level I*]). In patients with only low paraortic nodes as the site of distant spread, it is reasonable to consider para-aortic radiation with a boost to the nodes. Long term survival of patients with non-visceral IVB disease treated with radiotherapy, has been reported.

### **7.2.2 Brachytherapy (BT)**

Brachytherapy is an integral part of radiotherapy for carcinoma of the cervix, treating mainly the primary tumour. High doses of radiation can be delivered to the tumour while the surrounding normal tissues (e.g. rectum) are relatively spared. BT is usually given using either manual or remote after-loading techniques.

### **7.2.3 Radical radiotherapy**

Radical radiotherapy involves the combination of EBRT and brachytherapy. Hysterectomy should not be attempted if there is any doubt about achieving complete surgical removal of the cancer, as the inability to insert a uterine source significantly jeopardises the efficacy of brachytherapy.

### **7.2.4 Other Techniques.**

Parametrial boost is a controversial topic and must be evaluated on a patient-to-patient basis. The total parametrial dose from EBRT should not exceed 53 Gray.

Central shielding during part of EBRT may be useful in bulky tumours, as it allows a higher dose of radiation to be delivered by brachytherapy to the central tumour, and increased dose to the pelvic side walls. Although there are physical and geometrical considerations of dose integration by brachytherapy and EBRT, the results of treatment with simple midline central shielding are acceptable (Arai et al, 1992) [*Level II-2*].

#### **(i) Pre-operative radiotherapy**

Pre-operative radiotherapy has been advocated but the overall results seem similar to radiotherapy used alone (Mendenhall et al, 1997) [*Level II-2*], while the complication rate of pre-operative radiotherapy is unacceptably high (Maurice et al, 2000) [*Level II-2*]. As such it is not advocated.

(ii) . *Adjuvant radiotherapy*

Adjuvant post operative radiotherapy is recommended for patients whose primary therapy was surgical, in two scenarios:

- **Unfavourable Prognostic Factors:**

5

Following radical surgery, adjuvant chemo-radiotherapy is recommended where there are unfavourable histologic prognostic features namely :

1. Positive pelvic nodes (any number)
2. Positive or close resection margins
3. Evidence of microscopic parametrial tumour spread

(Peters et al, 2000; Landoni et al, 1997; Mendenhall et al, 1994) [*Level I*], Benedet et al, 2000). Adjuvant pelvic chemo-radiotherapy in these settings has shown survival benefit versus radiotherapy alone.

The other risk factors for pelvic relapse are **bulky tumours** more than 4 cm in diameter or lympho-vascular invasion. However, the use of chemo-radiotherapy in these categories of patients have not yet shown a survival benefit, although the risk of pelvic relapse is reduced with radiotherapy (Mendenhall et al, 1994) [*Level II-2*].

- **Incidentally Diagnosed Invasive Cervical Cancer**

Patients found to have invasive cervical cancer (> stage 1A1) after a simple hysterectomy for presumed benign disease, should be given post-operative radiation therapy, or radical parametrectomy and pelvic lymphadenectomy.

In the post-operative setting, the lack of the uterus hampers brachytherapy. The areas at risk of failure are the vaginal cuff and pelvis. Given the morbidity of a combined full radiotherapy treatment (EBRT & brachytherapy), pelvic radiation alone is recommended. The total pelvic dose may be increased to 48 – 51 Gy (Peters et al, 2000) [*Level I*]. Chemotherapy is used concurrently as in the EBRT protocol

### 7.3. Chemotherapy

Chemotherapy is a frequently used modality in cervical cancer. The uses of intravenous chemotherapy include :

- Neoadjuvant and adjuvant
- Concurrent with radiotherapy (Chemoradiation)
- Palliation

Intra-arterial chemotherapy is strictly experimental and not recommended apart from clinical trials.

### 7.3.1. Neoadjuvant and adjuvant chemotherapy

Neoadjuvant chemotherapy aims to reduce the tumour burden to facilitate surgery or radiotherapy. However, evidence from large randomised trials does not indicate benefits with respect to survival (Kumar et al, 1998; Tattersall et al, 1995; Sundfor et al, 1996; Chiara et al, 1994; Sardi et al, 1997; Souhami et al, 1991; Chang et al, 2000; Herod et al, 2000; Symonds et al, 2000) [*Level I*]. In fact, two trials have shown that neo-adjuvant chemotherapy prior to radiotherapy may be detrimental to patients leading to decreased survival (Tattersall et al, 1995; Souhami et al, 1997) [*Level I*]. Thus, although there is good response with chemotherapy, it has not resulted in improved survival or local control of the disease. Hence, neo-adjuvant chemotherapy should be carried out only within the context of a clinical trial.

In other tumour sites, adjuvant chemotherapy is often administered to eradicate possible micrometastases. However, there are no large randomised trials to address the benefit of adjuvant chemotherapy in cervical cancer (Tattersall et al, 1992) [*Level II-1*]. The trials on neo-adjuvant therapy also did not show a decrease in distant metastases suggesting a lack of effectiveness of chemotherapy for micrometastases (Tattersall et al, 1995; Sundfor et al, 1996; Chiara et al, 1994) [*Level II-1*]. As such, adjuvant chemotherapy should also be used only within the context of a trial.

### 7.3.2. Concurrent chemo-radiotherapy

Chemotherapy given concurrently with radiation may act synergistically to improve the efficacy of radiotherapy, as well as having independent cell cytotoxicity. Recent Phase III trials using cisplatin based chemotherapy concurrently with radiation have demonstrated increase in disease free states and improved overall survival (Whitney et al, 1999; Morris et al, 1999; Keys et al, 1999; Rose et al, 1999; Peters et al, 2000) [*Level I*]. This improvement was seen in stages IB2 – IVA in both the radical and adjuvant radiotherapy settings, with the relative risk of death being reduced by 30 – 40%. At present, all patients with squamous carcinomas stages IB2 - IVA, should be considered for concurrent chemo-radiotherapy unless contraindicated. These may include patients with impaired renal function, inadequate blood counts and very old or frail patients.

**Cisplatin** is the drug of choice for concurrent chemo-radiotherapy. Cisplatin combinations has not shown any particular advantage over cisplatin as a single agent and results in greater toxicity. The role of Carboplatin, administered concurrently with radiotherapy, is undefined, and cannot be recommended.

The details of chemotherapy are provided in Appendix 3.

## 8 SPECIAL SITUATIONS

### 8.1 Adenocarcinoma

The treatment for adenocarcinomas is similar to that for squamous carcinomas. Although adenocarcinomas may be more radio-resistant, post-radiation results are almost comparable to surgery at the early stages (Shingleton et al, 1995) [*Level II-1*]. The role of

concurrent chemo-radiotherapy in patients with adenocarcinoma is unclear, but in the event of uncertainty, it can be treated in a similar fashion as squamous cell carcinomas.

### 8.2 *Invasive Cervical Cancer During Pregnancy*

The management of invasive cancer of the cervix during pregnancy is similar to that of cancer in the non-pregnant patient. However, in pregnancy, the choice of treatment depends on the patient's wishes on continuation of the pregnancy. If fetal viability has not been achieved, and the lesion is stage 1A2, 1B or 2A, treatment may be radical hysterectomy and pelvic lymphadenectomy, with the fetus left in-situ. For patients whose pregnancies are close to fetal maturity, then caesarean section, radical hysterectomy and bilateral pelvic lymphadenectomy is the treatment of choice for early lesions. In patients with more advanced disease, radiotherapy may be considered.

## 9. RECURRENT CERVICAL CANCER AND PALLIATIVE TREATMENT

### 9.1. Recurrent Cervical Cancer

The treatment for recurrent cancer depends on the mode of primary therapy and the extent and site(s) of recurrence. A small proportion of patients with central recurrence may be candidates for radical treatment. Patients who have been treated initially with surgery may be considered for radiation while those who underwent radiation may be considered for surgery.

Radical surgery in recurrent cancer requires pelvic exenteration. Pelvic exenteration is usually limited to those with central recurrence. The peri-operative mortality is as high as 10% and the 5 year survival is about 40-50%. Pelvic exenteration should only be undertaken by trained gynaecological oncologists in centres with good anaesthetic and blood bank support.

In recurrent disease the same radical radiotherapy protocol could be used. The use of brachytherapy is limited to vaginal recurrences of less than 1 cm in diameter. With larger tumours, the dose distribution to the apex to the tumour is very low, and therefore, brachytherapy is not recommended. EBRT boost to the tumour would provide a better dose distribution. The total EBRT dose then should be at least 50 - 60 Gy. Interstitial implants could be considered for inferiorly located tumours.

### 9.2. Palliative Treatment

Cervical cancer is readily cured in the early stages. However, for patients with metastatic disease or with recurrent cancer, in very elderly patients, or those with extreme medical conditions, cure may not be realistic. Local symptoms usually include bleeding, discharge, pelvic pain as well as bowel and bladder symptoms. The symptoms of metastatic spread depend on the organs involved, usually lungs, liver and lymph nodes.

Apart from medical therapy, both radiotherapy and chemotherapy are useful modalities for palliation. Local symptoms may be improved by hypofractionated radiotherapy using tight margins around the tumour. Examples of possible schedules are:

- 35 Gy in 10 fractions over 2 weeks
- 40 Gy in 4 – 7 fractions over 4 weeks

For radiotherapy, the side-effects of therapy, as well as the inconvenience to the patient, must be taken into account. For bone metastases or swellings, hypofractionated schedules should also be used. Single fraction radiotherapy is preferred for bone metastases

There are many active chemotherapeutic drugs which can be used in cervical cancer. Treatment schedules are available in the Ministry of Health Chemotherapy Guidelines. Patients should be monitored closely to ensure that the desired palliation is not outweighed by the side effects.

## 10. FOLLOW UP

Most recurrences after surgical treatment of clinical cervical cancer develop in the pelvis within two years of primary treatment with 25% of recurrences developing in the upper part of the vagina and 27% of recurrences develop at distant sites, usually the lung or liver (Lahousen, 1993, Manetta et al, 1992 ). Approximately 40 to 45% of patients with invasive cervical cancer have recurrent or persistent disease after radiotherapy. Following radiation therapy, 43% of recurrences will be found in the parametrial area including the pelvic wall, 27% in the cervix, uterus or upper vagina, 6% in the lower two-thirds of the vagina and the remainder in distant or unknown sites (Graham, 1962) [Grade III.]

The objectives of the follow-up visits are as follows:

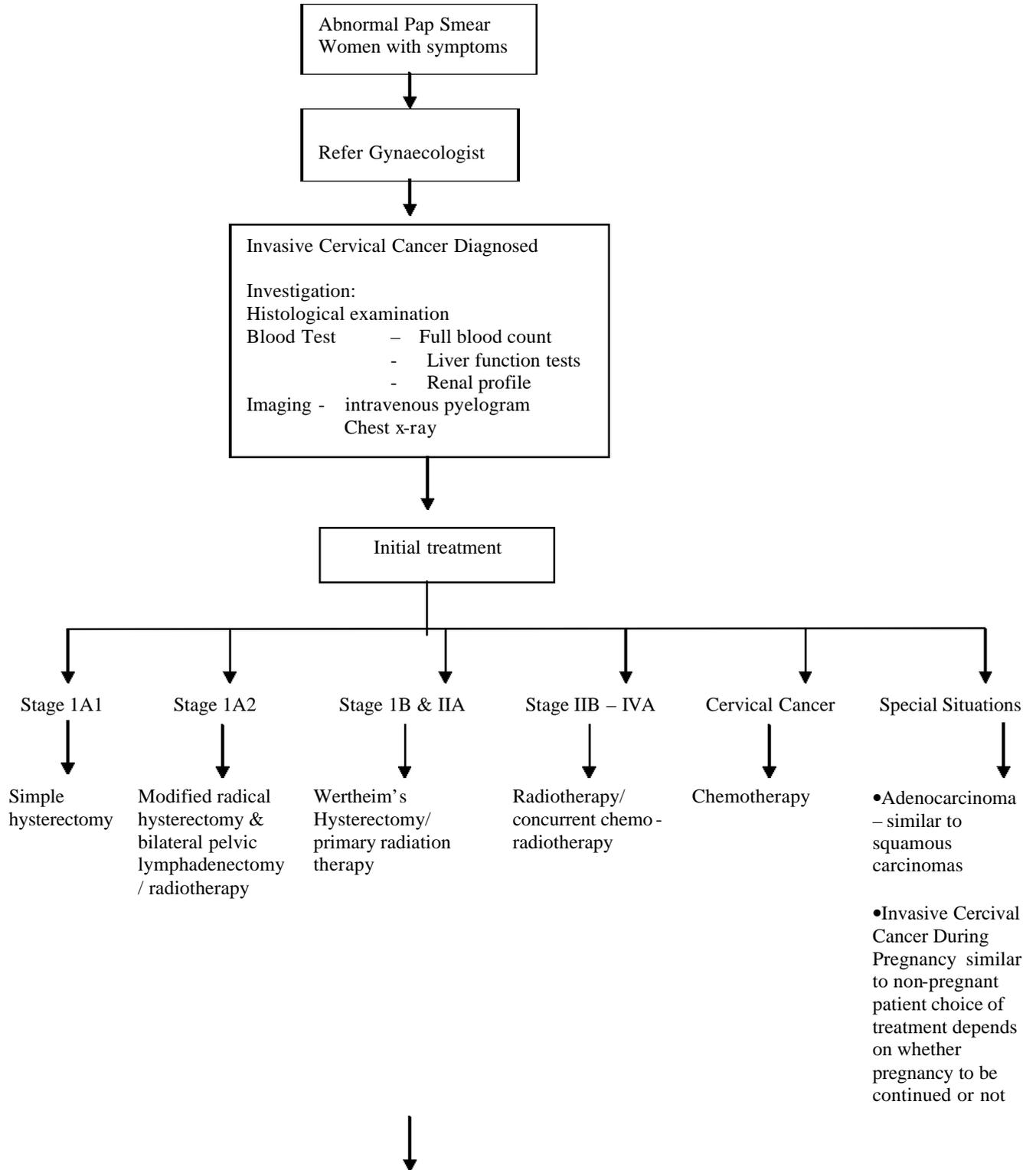
- To determine the patient's immediate response to the treatment employed
- Identify treatment related complications.
- Detection of persistent or recurrent disease

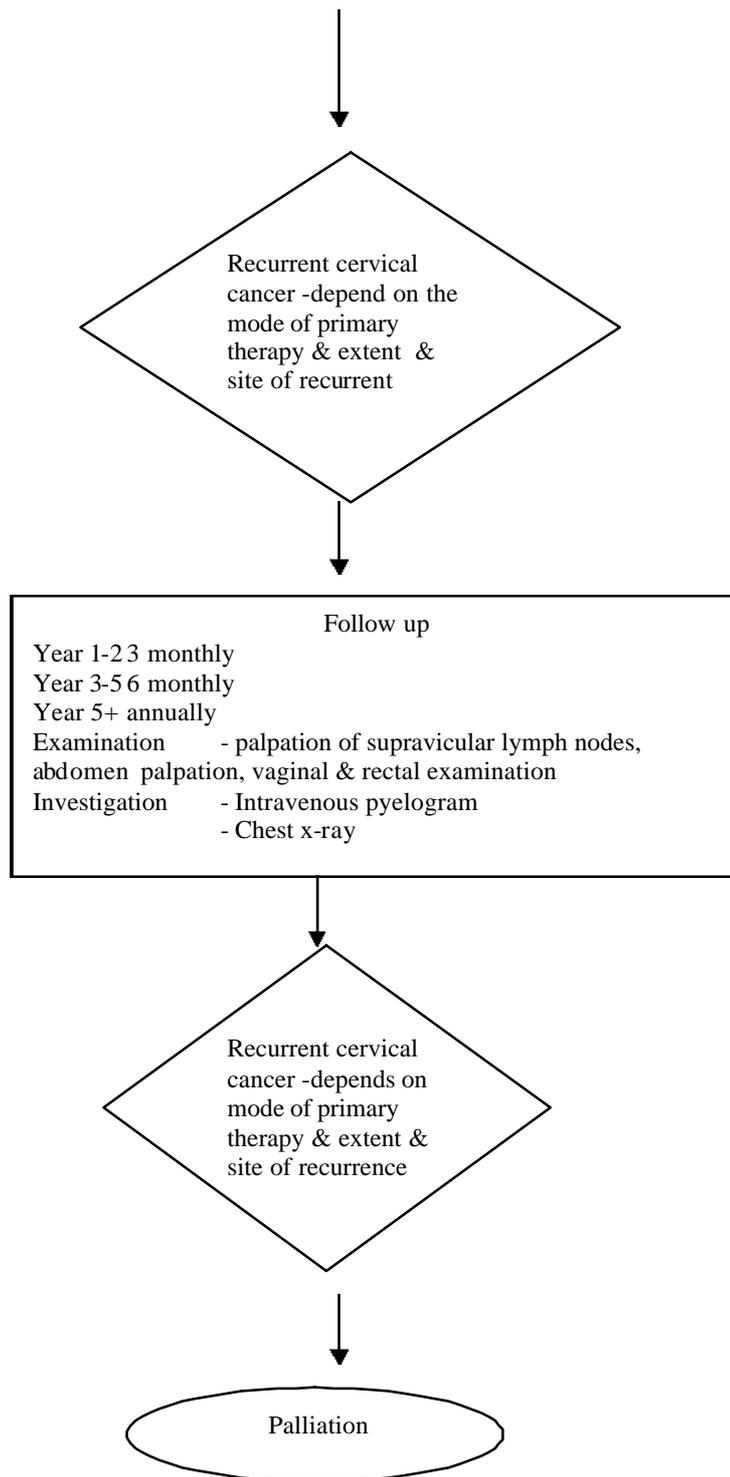
Close follow up should be directed to patients with poor prognostic factors and to detect early recurrence in those for whom potentially curable treatments exist. The ideal frequency of follow-up has not been evaluated. Below are the recommendations:

<b>Year 1 - 2</b>	every 3 months
<b>Year 3 - 5</b>	every 6 months
<b>Years 5+</b>	Annually

Each examination should include palpation of the supraclavicular lymph nodes, abdominal palpation for paraaortic enlargement, hepatomegaly and unexplained masses. Vaginal and rectal examination should be carried out to detect central and parametrial recurrence. Radical operations, which entail shortening of the vagina, can cause physical and psychosexual problems. Patients should be asked about constipation or voiding impairment. External stomas should be cared for appropriately (Lahousen, 1993)

## 11. ALGORITHM FOR MANAGEMENT OF ABNORMAL CERVICAL SMEAR





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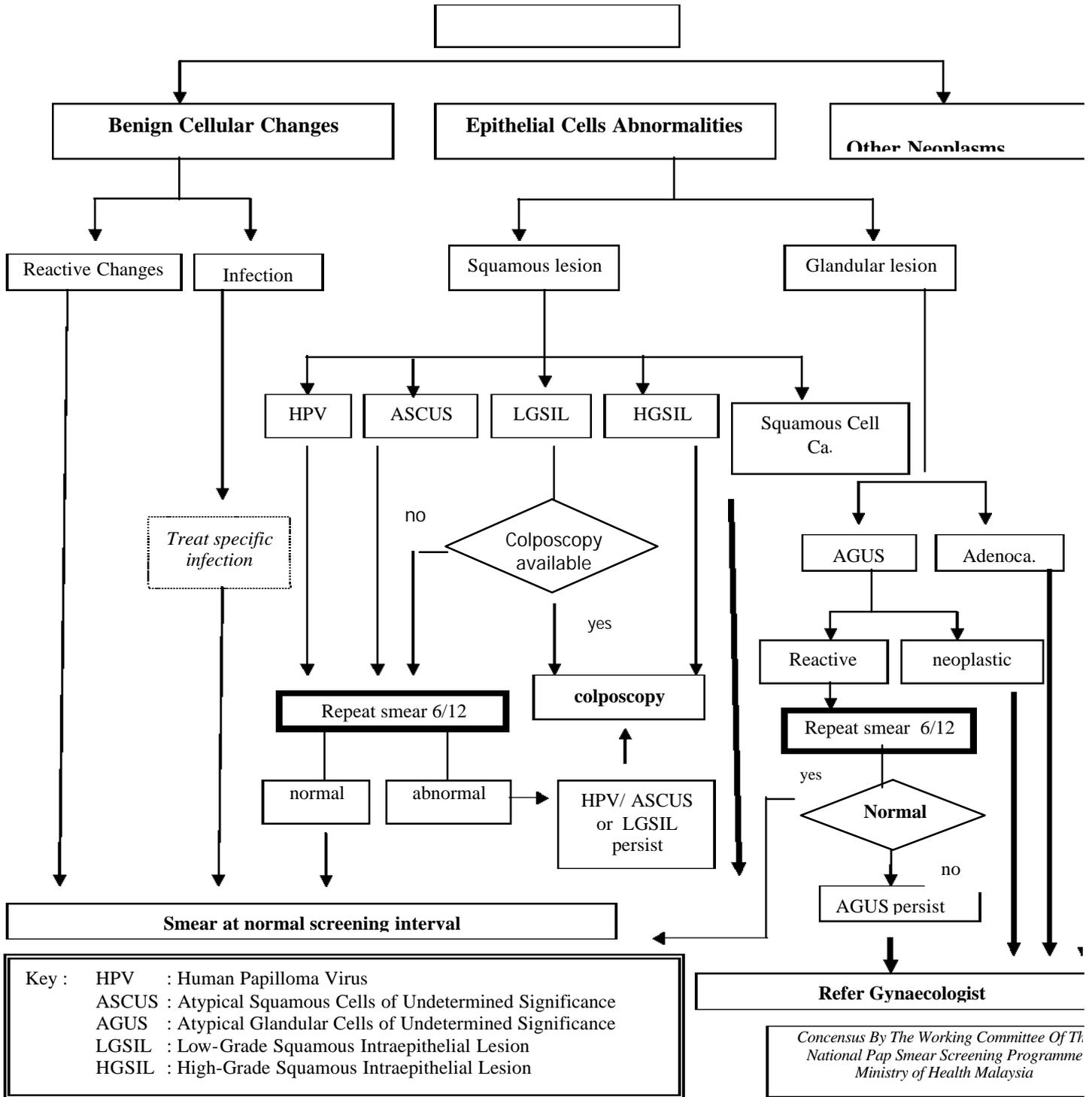
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**FLOW CHART FOR THE MANAGEMENT OF ABNORMAL**



**KEMENTERIAN KESIHATAN MALAYSIA  
PERKHIDMATAN PATOLOGI**

AB NO :

**BAHAGIAN 1a BUTIRAN PEMOHON**

I Hospital/Klinik.....

**BAHAGIAN III : RINGKASAN KLINIKAL**

i. No. Sitologi & No. Patologi terdahulu : .....

ii. Diagnosa terdahulu : .....

iii. Tarikh spesimen diambil :

iv. Tujuan smear diambil;

a. saringan  i. baru  ii. ulangan

b. diagnostik  i. baru  ii. ulangan

v. Tarikh Haid Akhir (THA) :

vi. Kontraseptif / Terapi :

a. ADR  d. Radiasi di bhg. pelvik

b. Hormon  e. Pembedahan Ginekologi

c. Kemoterapi nyatakan ; .....

vii. Status Hormon :

a. pre-menoposa  c. pospartum

b. hamil  d. menoposa

viii. Gejala / Tanda :

ix. Serviks :

a. biasa

b. luar biasa (nyatakan):.....

x. Jenis Persampelan :

a. Cervical Scrape

b. Endocervical Brush

c. Vault Smear

xi. Catatan tambahan :

.....  
.....  
.....

**BAHAGIAN 1b : BUTIRAN PEMOHON**

ii. Nama Doktor/Jururawat: .....

.....  
.....

**BAHAGIAN II : BUTIRAN PELANGGAN**

i. Nama Pelanggan : .....

ii. Umur : .....tahun

iv. Etnik:.....

v. No. K/P : (B).....(L).....

vi. Alamat : .....vii. No. Tel: (R):.....  
(P): .....

**BAHAGIAN IV : LAPORAN MAKMAL**

**ADEQUACY OF SPECIMEN**

**I. Satisfactory for evaluation :**

**II. Satisfactory for evaluation but limited by:**

i. inadequate squamous epithelial cells

ii. lack of endocervical cells/ Transformation zone component

iii. poor fixation, air drying, artifact

**III. Unsatisfactory for evaluation:**

i. broken slide

iii. obscuring blood, inflammation, thick areas

ii. scanty squamous epithelial component

iv. poor fixation, air-drying, artifact

**GENERAL CATEGORIZATION AND DISCRIPTIVE DIAGNOSIS**

**I. Within normal limits**

**II. Benign Cellular changes due to :**

**a. Reactive changes associated with:**

i. inflammation

iii. radiation

v. chemotherapy

ii. atrophy with inflammation

iv. IUCD

**b. Infection:**

i. Trichomonas vaginalis

iv. Bacteria – Actinomyces spp.

ii. Candida spp.

v. Cellular changes associated with HSV

iii. Predominance cocco bacilli

vi. Others (specify):.....

**III. Epithelial Cells abnormalities :**

**a. Squamous Cell:**

i. Atypical Squamous Cells of Undetermined Significance (ASCUS)

iv. High Grade Squamous Intraepithelial Lesion (HGSIL)

ii. Human Papilloma Virus (HPV)

v. Squamous cells carcinoma (CA)

iii. Low Grade Squamous Intraepithelial Lesion (LGSIL)

**b. Glandular Cell:**

i. Endometrial cells, benign in postmenopausal

iv. Endometrial adenocarcinoma (CA)

ii. Atypical glandular cells of undetermined significance (AGCUS)

v. Extruterine adenocarcinoma (CA)

iii. Endocervical adenocarcinoma (CA)

vi. Adenocarcinoma (CA)

**IV. Other Neoplasms: (specify) .....**

**CONCLUSION:** .....

**RECOMMENDATIONS/COMMENTS:** .....

Tarikh Laporan :

## Radiotherapy

### 1. External beam radiotherapy (EBRT)

The target volume for EBRT is the primary tumour and pelvic nodes. High energy photons > 6 MV are generally preferred, as a better dose distribution can be achieved. The 4-field technique is preferred with the following exceptions:

- Small separation - 18 cm or less
- Tumour extends posteriorly towards the rectum

For the 4-field technique, target volume should be marked to cover this adequately with total isodose. This ensures uniformity, as dose prescription is to either an isodose contour, or preferably, to the ICRU beam intersection point i.e. isocentre. In the event of uncertainty of exact tumour extent, it is better to use the Antero-Posterior / Postero-Anterior (AP/PA) fields.

#### *Volume of treatment*

Superior : L5 / S1  
 Inferior : Obturator foramen or lowest extent of tumour (whichever is lower)  
 Lateral : 1 cm beyond pelvic brim (1.5 – 2 cm for field border)  
 Anterior : mid-way through symphysis pubis  
 Posterior : S2 / S3 junction

#### *Other Techniques.*

Central shielding during part of EBRT may be useful in bulky tumours, as it allows a higher dose of radiation to be delivered by brachytherapy to the central tumour, and increased dose to the pelvic side walls. Although there are physical and geometrical considerations of dose integration by brachytherapy and EBRT, the results of treatment with simple midline central shielding are acceptable (Arai T et al, 1992).

#### *Dose prescription*

- Dose : 45 – 50.4 Gy
- Fractions : 25 - 28
- Prescription point : Isocentre or Mid-plane

### 2. Brachytherapy

Brachytherapy can be divided into 3 groups according to the dose rate of radiation treatment as illustrated in the table below:

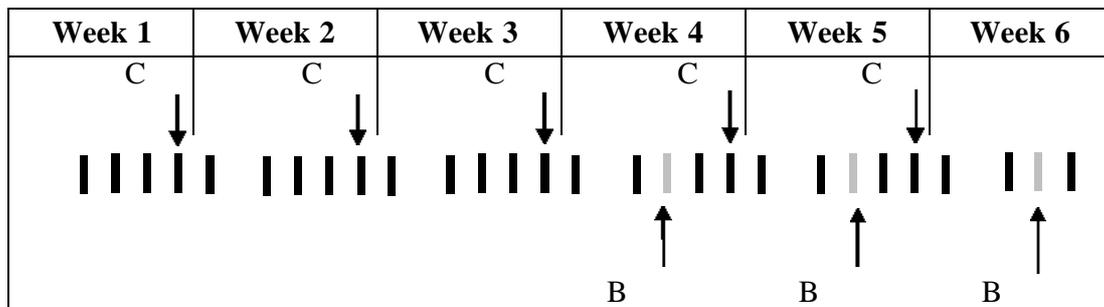
Type of Brachytherapy	Dose rate (Gy/hr.)
Low Dose Rate (LDR)	< 2
Medium Dose Rate (MDR)	2 - 12
High Dose Rate (HDR)	> 12

With adequate dose prescription, all 3 modalities result in similar overall survival rates. Since the HDR require several fractions of treatment, it is important to ensure that the overall treatment time is not prolonged, as it may compromise survival. Treatment time should be kept below 7 weeks (Perez C et al, 1995) (*Level II-2*). Therefore, the HDR fractions should be interdigitated in between EBRT ( Nag S et al, 2000) (*Level II-1*).

The total dose to Manchester Point A from EBRT and brachytherapy should be the equivalent of at least 75 Gray at low dose rate.

In the post-operative setting, the dose distribution from brachytherapy is not ideal. The dose prescription point is to a specified distance to the mucosa, usually 0.5 cm. In post-surgery recurrent tumours, the use of brachytherapy should be limited to small tumours, and EBRT boost maybe more appropriate (Ito H et al, 1997) (*Level II-2*).

There should be no teletherapy treatment on the day of brachytherapy. A suggested radiotherapy scheme is presented below. Similar treatment plans are acceptable.



| = Teletherapy  
 C = Chemotherapy  
 B / | = HDR Brachytherapy

In the case of LDR brachytherapy, the insertion should be done immediately after completion of radiotherapy. If fractionated LDR treatment is used, then it could be integrated into the EBRT scheme or spaced a week apart at the end.

Patients who are unsuitable for brachytherapy, or in whom an insertion is technically not possible, should have a planned boost field to the primary tumour. In such cases, the total EBRT dose should be at least 60 Gy.

**Chemotherapy Regime (Concurrent Chemoradiotherapy only)**

Prior to chemotherapy, all patients must have

- Full blood count
- Renal profile

There must be adequate blood counts and renal function before chemotherapy is administered.

Cisplatin based chemotherapy is recommended as standard, with Cisplatin 25 – 40 mg / m<sup>2</sup> weekly (or an absolute dose of 50 mg for convenience) being preferred. The following are suggested regimes :

	<b>Drugs</b>	<b>Dose (mg / m<sup>2</sup>)</b>	<b>Days</b>	<b>Length of Cycle</b>
1	Cisplatin 5-Fluorouracil	70 1000	1 1 - 4	3 weeks
2	Cisplatin 5-Fluorouracil	50 1000	1 1 - 4	4 weeks
3	Cisplatin	40	1	weekly

**Hydration:** - 500 ml Normal Saline over 1 hour  
 - 50 mg cisplatin in 1 liter Normal Saline over 2 hours  
 - 500 ml Normal Saline over 1 hour

This short hydration regime is only suitable for low dose Cisplatin of around 30 mg / m<sup>2</sup>, and is NOT SUITABLE for higher doses. Other hydration regimes are acceptable but it must be noted that patients are to have radiotherapy on the same day. Patients need to maintain oral fluid intake during this period.

**Anti-emetics:** Granisetron 1mg IV plus Dexamethasone 12mg IV (Gralla RJ et al, 1999[Level I])

(an alternate 5-HT3 antagonist can also be used)

Patients are to be given the following drugs for 3 days to take home:

- Dexamethasone 2 mg tds
- Metoclopramide 20 mg tds

Other anti-emetics are also acceptable but should include steroids.