Pan-Birmingham NHS
Cancer Network

Coversheet for Network Site Specific Group Agreed Documentation

This sheet is to accompany all documentation agreed by Pan Birmingham Cancer Network Site Specific Groups. This will assist the Network Governance Committee to endorse the documentation and request implementation.

Document Title	**Guidelines for the Management of Cervical Cancer**
Document Date	December 2007
Document Purpose	This guidance has been produced to support the following: • The management of patients with suspected Cervical Cancer • The management of patients diagnosed with Cervical Cancer
Authors	1 David Luesley Consultant Gynaecologist 2 Lara Barnish Project Lead 3 Suhail Anwar Consultant Clinical Oncologist
References	The International Federation of Gynaecology and Obstetrics (**FIGO**), 2000. **Staging classifications and clinical practice guidelines of gynaecological cancers** (pages 6-25). http://www.figo.org .
Consultation Process	Consultation was via the authors, the Gynae Network Site Specific Group, the Chemotherapy Network Site Specific Group and Oncologists.
Review Date (must be within two years)	February 2011
Approval Signatures: Network Site Specific Group Clinical Chair	
Date Approved by Network Governance Committee	20.02.08

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Guidelines for the Management of Cervical Cancer

Version History

Version	Date Issued	Brief Summary of Change
0.1	19.04.2005	First draft presented at NSSG (DML)
0.2	03.10.05	Draft developed and reworked into document template. (LB).
0.3	06.10.05	Draft following mtg (DML and LB)
0.4	07.11.05	Following Dr Anwar meeting
0.5	22.11.05	With Dr Anwar comments – for presentation at NSSG
0.6	06.12.05	Following discussion at NSSG
0.7	14.01.06	For final approval from NSSGs: Gynae, Cellular Pathology, Radiology and the Clinical/Medical Oncologists
0.8	31.01.06	Following consultation (SA and IF comments) and NSSG Discussion. For consideration by the Clinical Governance Committee.
0.9	13.02.06	For Submission to Clinical Governance
1.1	30.10.07	With James Nevin and Indy Fernando (12.11.07) comments for review by Gynae NSSG
1.1	24.11.07	Circulated to NSSG for comments
1.1	06.12.07	Discussed at NSSG, for circulation to the Oncologists and Chemotherapy NSSG. Approved at the Gynae NSSG
1.2	13.12.07	With comments following consultation with the Oncologists and Chemotherapy NSSG
2.0	20.02.08	Endorsed by the Governance Committee

Changes made during Review in 2007/2008

- *Change 1 – (Page 3) Deleted "From September 2005"*
- *Change 2 – (Page 3) Deleted "The capacity and expertise will be available in the cancer centre from 1st September 2005"*
- *Change 3 – (Page 4) added "(via SLA at Birmingham Women's Hospital)"*
- *Change 4 – (Page 5)added "or close margins less than or equal to 5mm,"*
- *Change 5 – (Page 5) added "Indications for post-wertheims chemo XRT include the following: nodal positivity, parametrial positivity, a Delgado score of more than 120 in patients with negative nodes and uninvolved parametria."*
- *Change 6 – (Page 5) added "though patients may be considered for the CX2 trial and commence chemotherapy prior to chemo-irradiation."*
- *Change 7 – (Page 6) deleted "preferences" and added "Guidelines for the Follow up of Gynaecological Malignancies. Patients who have been recruited into a clinical trial will be followed up as per the protocol."*

Scope of the Guideline

This guidance has been produced to support the following:

- The management of patients with suspected Cervical Cancer
- The management of patients diagnosed with Cervical Cancer

Guideline Background

In cancer care there have been a number of policy documents published, as well as those produced by professional bodies, that describe the care and treatment individuals with cancer should receive. Some of these documents also state that network wide guidance should be produced.

This guideline has been written in response to the above and aims to make sense of these documents within the context of the Pan Birmingham Cancer Network, ensuring that more up to date research, current thinking, and local expert opinion have been incorporated.

All Trusts undertaking gynaecological surgery in the Pan Birmingham Cancer Network are recognised as cancer units. One Trust (Sandwell and West Birmingham Hospital NHS Trust (SWBH); City Hospital Site) is recognised as the Gynaecological Cancer Centre. Our objectives are in line with National Guidance in that all women with cervical cancer greater than stage 1a will be managed within the Gynaecological Cancer Centre.

Guideline Statements

<u>Referral</u>

- In the following circumstances women should be referred to a gynaecologist assessment service
    - post coital bleeding
    - inter menstrual bleeding
    - persistent vaginal discharge
    - where the cervix looks or feels abnormal (even if the cervical smear is reported to be negative)

- Where the clinical suspicion of cancer is high (a lesion suspicious of cancer on speculum examination) a direct referral to the cancer unit assessment clinic should be made. **A previous negative smear result should not delay referral** when the clinician suspects malignancy based on clinical/speculum examination. **A cervical smear should not be taken** in these cases.

- When cancer is suspected on cervical smear results the patient should be referred to the colposcopy clinic in the local cancer unit.

Diagnosis

Within Pan Birmingham Cancer Network all cervical cancers are diagnosed and staged in the cancer units. All patients are discussed in the MDT and those with stage greater than 1a, identified as requiring surgery, are referred to the gynaecological cancer centre (SWBHT). Where medical management is indicated the patients are referred directly to the clinical oncologist following discussion with the centre gynae-oncology surgeon.

When microinvasive cervical cancer (stage 1a1 and 1a2) is suspected at colposcopic assessment

- A loop or cone should be carried out by an accredited colposcopist in the cancer unit. Directed or punch biopsies are unreliable for the diagnosis of stage 1a cervical cancer.
- When excision is incomplete one further excision should be attempted. If excision remains incomplete the tumour should be considered as stage 1b and the patient referred to the cancer centre.

When a cancer > stage 1a or an adenocarcinoma is suspected

- A large representative (cone or wedge) biopsy should be performed.

A large representative biopsy is ideal. This need not totally excise the lesion as an attempt to do so may provoke unwanted morbidity and delay definitive treatment. Directed biopsies may provide the diagnosis in large clinically obvious lesions. Necrotic tissue from the tumour may not be sufficient to confirm the diagnosis.

Pathology: biopsy specimens should be examined by a designated pathologist with a special interest in gynaecological malignancy. Any specimens that reveal microinvasive carcinomas should be sent to the designated pathologist at the cancer centre (via SLA at Birmingham Women's Hospital).

Staging

Formal staging includes EUA, Biopsy, Cystoscopy, Sigmoidoscopy and Chest X-ray. Decisions regarding which investigations are required to reliably stage the patient and investigate co-morbidity should be based on individual assessment and MDT discussion of each patient and her tumour. For example, sigmoidoscopy would not be warranted in the case of a small 1cm lesion of the anterior cervical lip. Although not formally part of FIGO staging, MRI is recommended in most cases to assess tumour size and possible extracervical extension (this is the subject of a current audit).

Treatment

- Premenopausal women with early stage disease, for whom treatment is likely to affect fertility, should have fertility sparing options discussed.

Stage 1a

A cone biopsy may be sufficient both for the diagnosis and treatment when there is no evidence of tumour at the margins of the sample. If the biopsy results suggest a higher

stage tumour, or if there are poor prognostic factors (e.g. LVS involvement), the patient should be referred to the cancer centre.

All patients should be discussed at the MDT (with the cone biopsy results) and decisions re further treatment options made on an individual basis.

Cases should be considered for lymph node removal based on adverse pathological factors (e.g. LVS invasion). NB - there is weak evidence to support this and decisions need to be based on an individual patient basis.

Stage 1a2
If LVS invasion is noted on histology after TAH, adjuvant radiotherapy to the pelvis should be considered (as there is a 10-15% risk of nodal metastases).

Stage 1b and IIa
Treatment is either surgery (hysterectomy with pelvic lymphadenectomy) or chemoradiotherapy. Radiotherapy (external beam and brachytherapy) alone is also an option. Factors influencing treatment choice include tumour bulk, likelihood of requiring adjuvant radiation (in the case of surgery), performance status, fertility status, patient choice and co-morbidities.

Currently available evidence suggests that both radical surgery and radical radiotherapy are equally effective but have different morbidities. Chemoradiation may offer improved survival when compared to radiotherapy alone although the morbidity is greater. As yet, there has been no formal comparison between chemoradiation and radical surgery.

Incomplete responses to radiotherapy may be considered for salvage surgery. If the available clinico-pathological information at the outset suggests that post-operative radiation is going to be likely (adverse pathological factors such as neuroendocrine elements, bulky tumours, radiological suspicion of nodal involvement), then radiotherapy should be considered as the first line of management.

Adjuvant radiotherapy (following surgery) should be avoided if possible although it is conceded that there are instances when this could not have been predicted from the pre-treatment assessment (positive **or close margins less than or equal to 5 mm**, microscopic involvement of pelvic lymph nodes or parametrium and lymphovascular space invasion). Indications for post-wertheims chemo XRT include the following: nodal positivity, parametrial positivity, a Delgado score of more than 120 in patients with negative nodes and uninvolved parametria.

Stages IIb, IIIa, IIIb and IVa
Concurrent Chemoradiation or Radiotherapy (if unfit for chemotherapy) is the treatment of choice, though patients may be considered for the CX2 trial and commence chemotherapy prior to chemo-irradiation. Pelvic radiation may commence during or after chemotherapy. Some patients may require more chemotherapy following chemoradiation. The choice of radiotherapy or chemoradiotherapy depends on many factors including the co-morbidity of the patients and the extent of the disease. In some cases of locally advanced disease the aim of the treatment may be palliation.

Extra Pelvic Disease/Recurrent disease

This is incurable disease and should be dealt with sensitively as many patients are very young or at least with young families. The choices, however, are limited. The aim is palliation and possible prolongation of life.

All patients must be referred to palliative care teams as early as possible.
One or more of the following can be considered according to a particular patient's situation/needs:

1. Palliative chemotherapy
2. External beam radiotherapy
3. Brachytherapy

Histological variants such as small cell, neuroendocrine, clear cell and serous tumours should be considered for chemotherapy in addition to any surgical/radiotherapy intervention.

Patients identified as requiring surgical treatment for recurrent cancer should be managed under the care of the cancer centre.

Trials

Patients may be considered for entry into Regional, National and International trials approved by the relevant ethics committees. Ethics approval is being sought for a Phase II study of weekly neoadjuvant chemotherapy (Paclitaxel and Carboplatin) followed by radical chemoradiation for locally advanced cervical cancer (An NCRN adopted trial, EUDRACT no. 2005-000134-20)

Follow-up

Patients treated at the cancer unit should be followed up at the cancer unit. Those treated at the centre receive one follow up appointment at the centre and are then offered either centre or unit based follow up according to the Guidelines for the Follow up of Gynaecological Malignancies. Patients who have been recruited into a clinical trial will be followed up as per the protocol.

Appendix 1: Staging of Cervical Cancer

FIGO Stages		TNM Categories
	Primary tumour cannot be assessed No evidence of primary tumour	TX T0
0	Carcinoma insitu (preinvasive cancer)	Tis
I IA IA1 IA2 IB IB1 IB2	Cervical carcinoma confined to uterus (Extension to corpus should be disregarded). Invasive carcinoma diagnosed only by microscopy. All macroscopically visible lesions – even with superficial invasion – are Stage 1B/T1b. Stromal invasion no greater than 3.0mm in depth and 7.0 mm or less in horizontal spread. Stromal invasion more than 3.0 mm and not more than 5.0 mm with a horizontal spread 7.0 mm or less[a]. Clinically visible lesion confined to the cervix or microscopic lesion greater than 1A2/T1a2. Clinically visible lesion 4.0 cm or less in greatest dimension Clinically visible lesion more than 4com in greatest dimension	 T1 T1a T1a1 T1a2 T1b T1b1 T1b2
II IIA IIB	Tumour invades beyond the uterus but not to pelvic wall or to lower third of the vagina Without parametrial invasion With parametrial invasion	 T2 T2a T2b
III IIIA IIIB	Tumour extends to pelvic wall and/or involves lower third of vagina and/or causes hydronephrosis or non-functioning kidney Tumour involves lower third of vagina no extension to pelvic wall Tumour Extends to pelvic wall and/or causes hydronephrosis or non-functioning kidney	 T3 T3a T3b
IVA	Tumour invades mucosa of bladder or rectum and/or extends beyond true pelvis[b]	 T4
IVB	Distant metastasis	M1

[a] The depth of invasion should not be more than 5mm taken from the base of the epithelium, either surface or glandular, from which it originates. The depth of invasion is defined as the measurement of the tumour from the epithelial-stromal junction of the adjacent most superficial epithelial papilla to the deepest point of invasion. Vascular space involvement, venous or lymphatic, does not affect classification.

[b] The presence of bullous oedema is not sufficient to classify a tumour as T4

Monitoring of the Guideline

Implementation of the guidance will be considered as a topic for audit by the NSSG in 2011.

References

The International Federation of Gynaecology and Obstetrics (**FIGO**), 2000. **Staging classifications and clinical practice guidelines of gynaecological cancers** (pages 6-25). http://www.figo.org .

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Date Approval by the Clinical Governance Team: Date: 20 February 2008

Approval Signatures

Pan Birmingham Cancer Network Governance Committee Chair

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Name: David Luesley Signature Date: 6 December 2007

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To be reviewed by the NSSG in 2011