子宮頸癌診療指引

婦癌多專科團隊

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2015 年 12 月修訂

參考資料：

Cervical Cancer Guidelines V2.2015

全民健康保險藥品給付規定行政院衛生署一零四年版(20928_1)

Physicians' Cancer Chemotherapy Drug Manual 2010

LCIS = Lobular carcinoma in situ

DCIS = Ductal carcinoma in situ

(+) = positive

(-) = Negative

LN = lymph node

R/T = radiation therapy

c With

s = without

ALP= alkaline phosphatase

PBI = partial breast irradiation

CR =Complete response

PD =Progressive disease

LVSI =Lymphovascular space invasion

WAKE UP

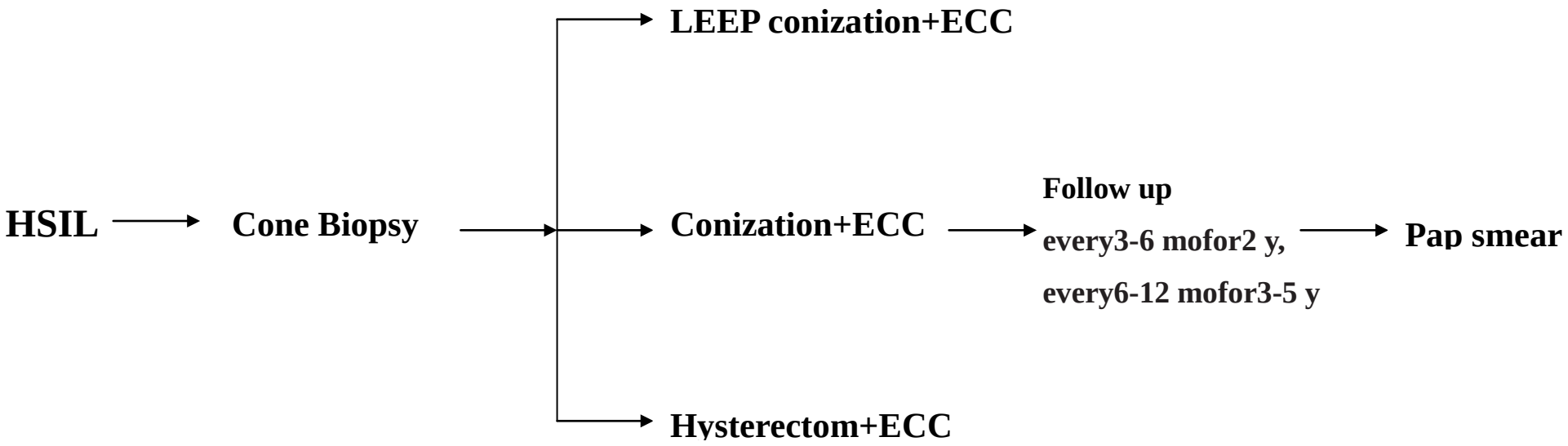
- History
- Physical examination
- Complete blood count(CBC) & Platelet
- Pathologic Review
  - ➢ Cervical biopsy or cone biopsy
- Liver function test/Renal function studies
- Imaging

(Optional for ≦ stage IB1):

- ➢ Chest x-ray
- ➢ CT
- ➢ MRI as indicated

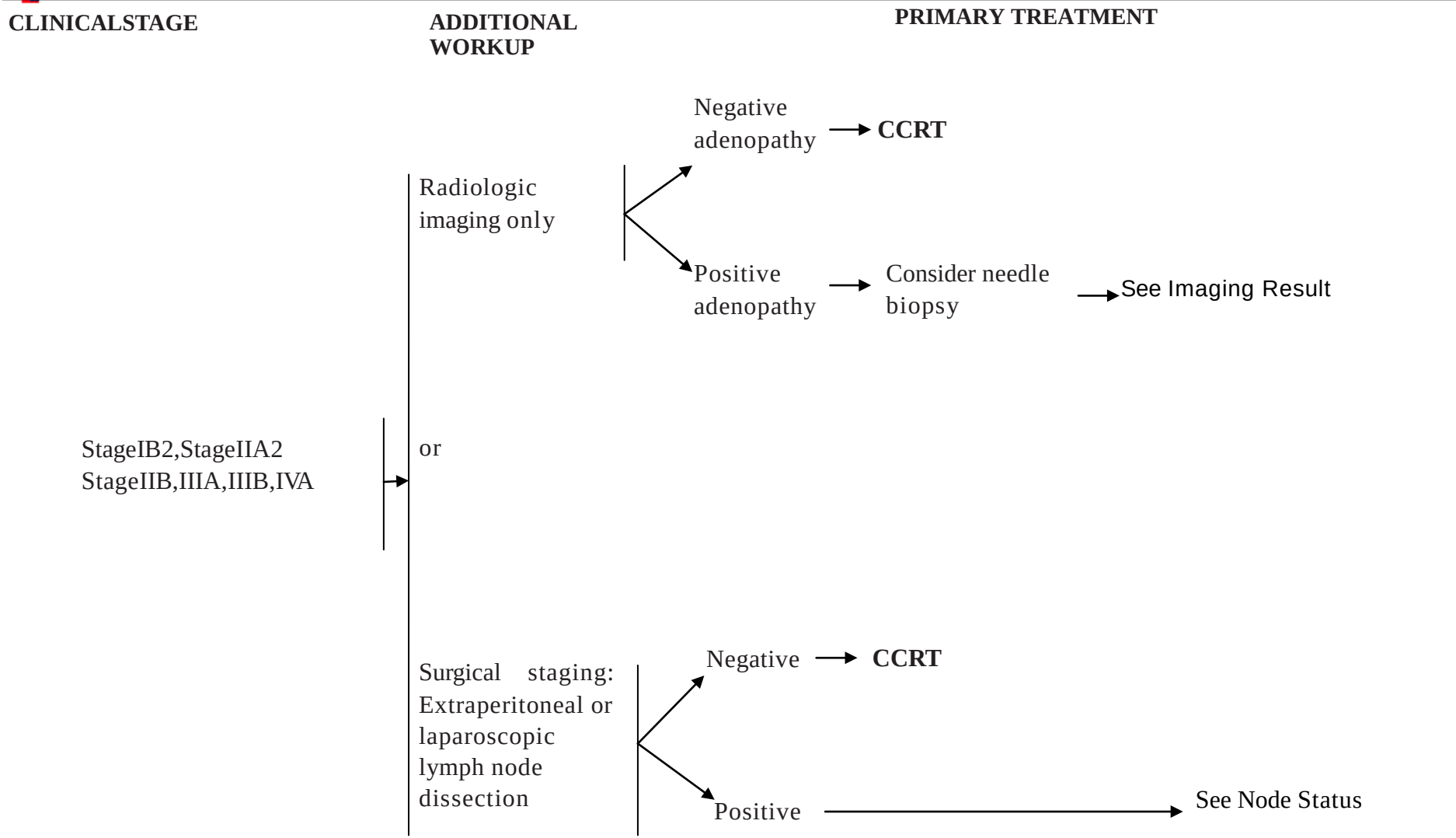
→ **CLINICAL STAGE**

TREATMENT OF HSIL (CIN III)



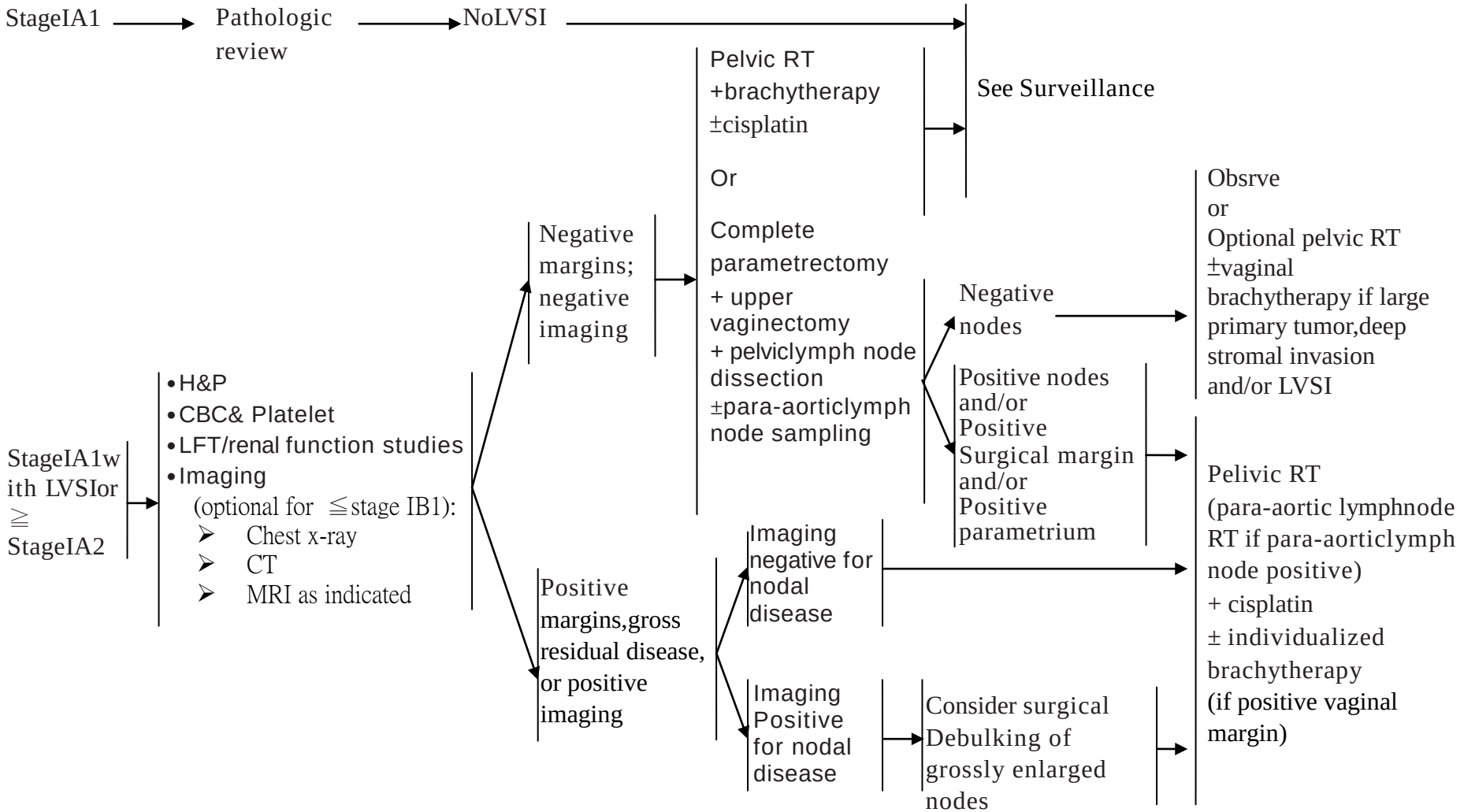
CLINICALSTAGE		PRIMARY TREATMENT	
Stage IA1 (No LVSI)	Fertility sparing	**Cone biopsy with negative margins:** (preferably a non-fragmented specimen with 3-mm negative margins) (If positive margins, repeat cone biopsy or perform trachelectomy)	Surveillance
	Non-Fertility sparing	**Cone biopsy with Negative margins and inoperable:**Observe	
		Cone biopsy with Negative margin sandoperable: Extrafascial hysterectomy	
		Cone biopsy with Positive margins for dysplasia for carcinoma: modified radical hysterectomy+ pelvic lymph node dissection	Surgical Findings
Stage IA1 (LVSI) and Stage IA2	Fertility sparing	1.Negative margins Cone biopsy is enough.	Surveillance
		2.If positive margins, repeat cone biopsy or perform trachelectomy+ pelvic lymph node dissection ±para-aortic lymph node sampling(2B)	
		3.Radical trachelectomy + pelvic lymph node dissection (± para-aortic lymph node sampling)	
	Non-Fertility sparing	Pelvic RT+brachytherapy(total point A dose 70~80Gy)	
		Modified radical hysterectomy + pelvic lymph node dissection ± para-aortic lymph node sampling	Surgical Findings

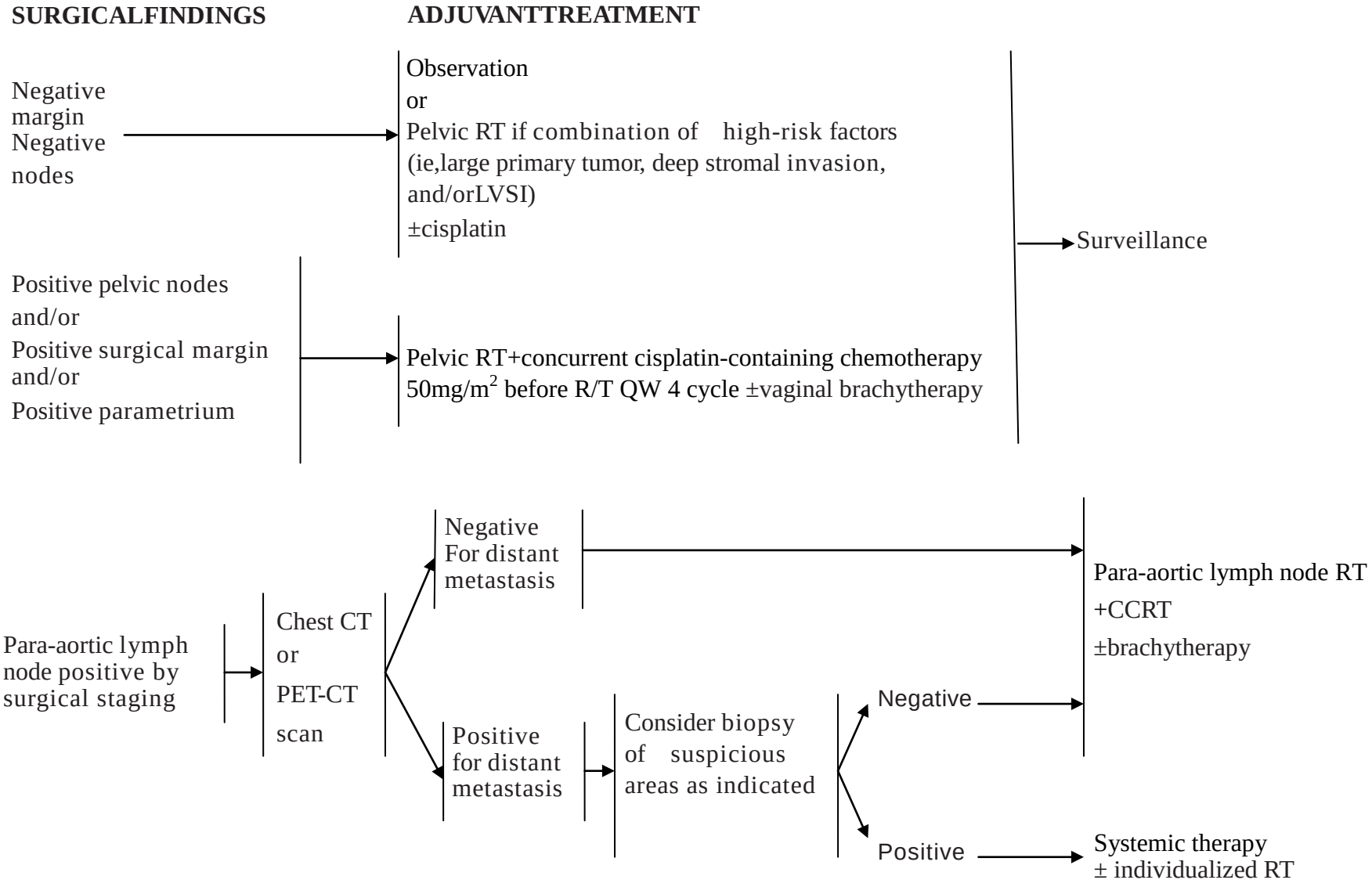
CLINICALSTAGE		PRIMARY TREATMENT	
Stage IB1	Fertility sparing	Radical trachelectomy + pelvic lymph node dissection ± para-aortic lymph node sampling	Surveillance
	Non-Fertility sparing	Radical hysterectomy + pelvic lymph node dissection ± para-aortic lymph node sampling	Surgical Findings
Stage IIA1	Non-Fertility sparing	Or Pelvic RT +brachytherapy(total point A dose 80~85Gy) ±concurrent CCRT	Surveillance
Stage IB2 and Stage IIA2	Non-Fertility sparing	Definitive Pelvic RT + cisplatin +brachytherapy(total point A dose ≧85GY)	Surveillance
		Radical hysterectomy + pelvic lymph node dissection ± para-aortic lymph node sampling	Surgical Findings
		Pelvic RT + cisplatin +brachytherapy(total point A dose 75-80GY) +adjuvant hysterectomy	Surveillance


CLINICALSTAGE
ADDITIONAL WORKUP
PRIMARY TREATMENT
StageIB2,StageIIA2
StageIIB,IIIA,IIIB,IVA
Radiologic imaging only
Negative adenopathy
CCRT
Positive adenopathy
Consider needle biopsy
See Imaging Result
or
Surgical staging: Extraperitoneal or laparoscopic lymph node dissection
Negative
CCRT
Positive
See Node Status

INCIDENTAL FINDING OF INVASIVE CANCER AT SIMPLE HYSTERECTOMY

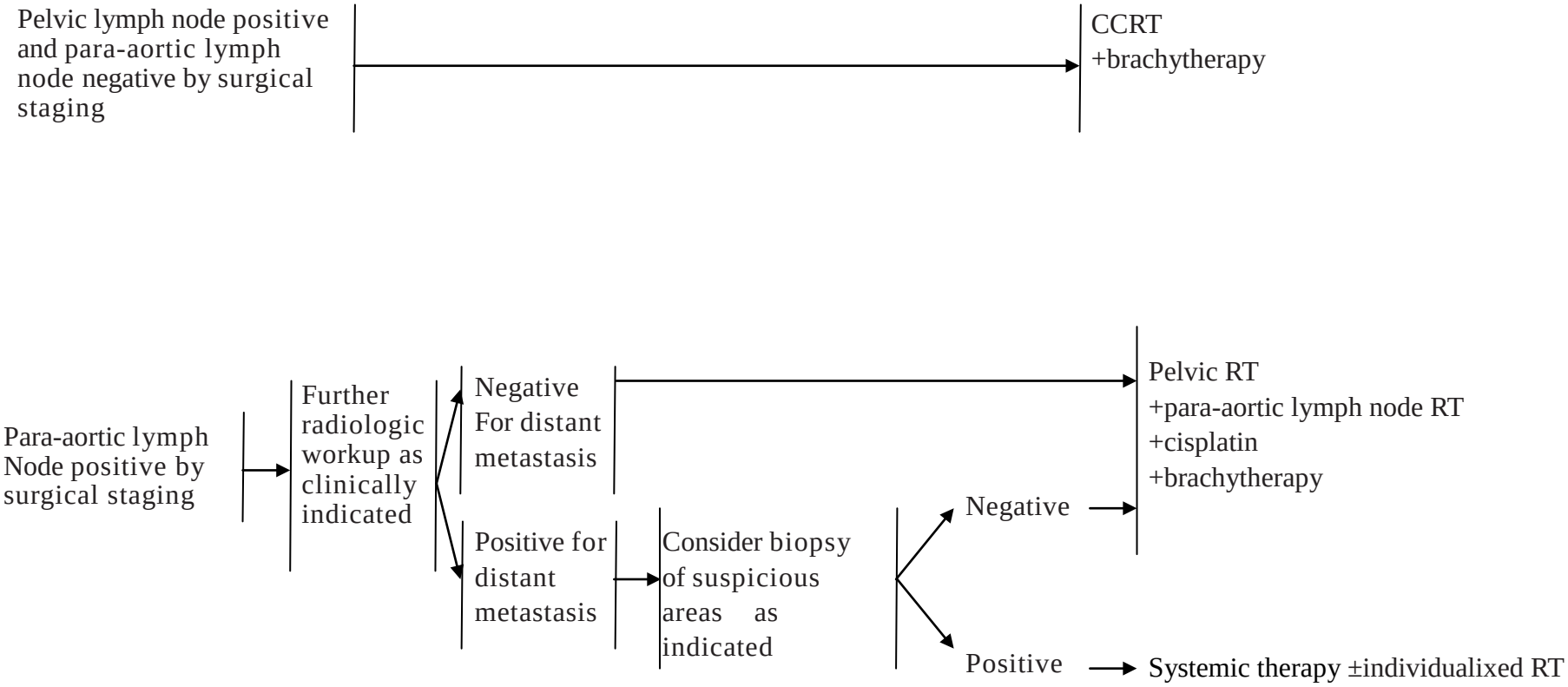
PRIMARY TREATMENT




SURGICALFINDINGS
ADJUVANTTREATMENT
Negative margin
Negative nodes
Observation
or
Pelvic RT if combination of high-risk factors (ie,large primary tumor, deep stromal invasion, and/orLVSI)
±cisplatin
Surveillance
Positive pelvic nodes
and/or
Positive surgical margin
and/or
Positive parametrium
Pelvic RT+concurrent cisplatin-containing chemotherapy
50mg/m2 before R/T QW 4 cycle ±vaginal brachytherapy
Para-aortic lymph node positive by surgical staging
Chest CT
or
PET-CT
scan
Negative
For distant
metastasis
Positive
for distant
metastasis
Consider biopsy
of suspicious
areas as indicated
Negative
Positive
Para-aortic lymph node RT
+CCRT
±brachytherapy
Systemic therapy
± individualized RT

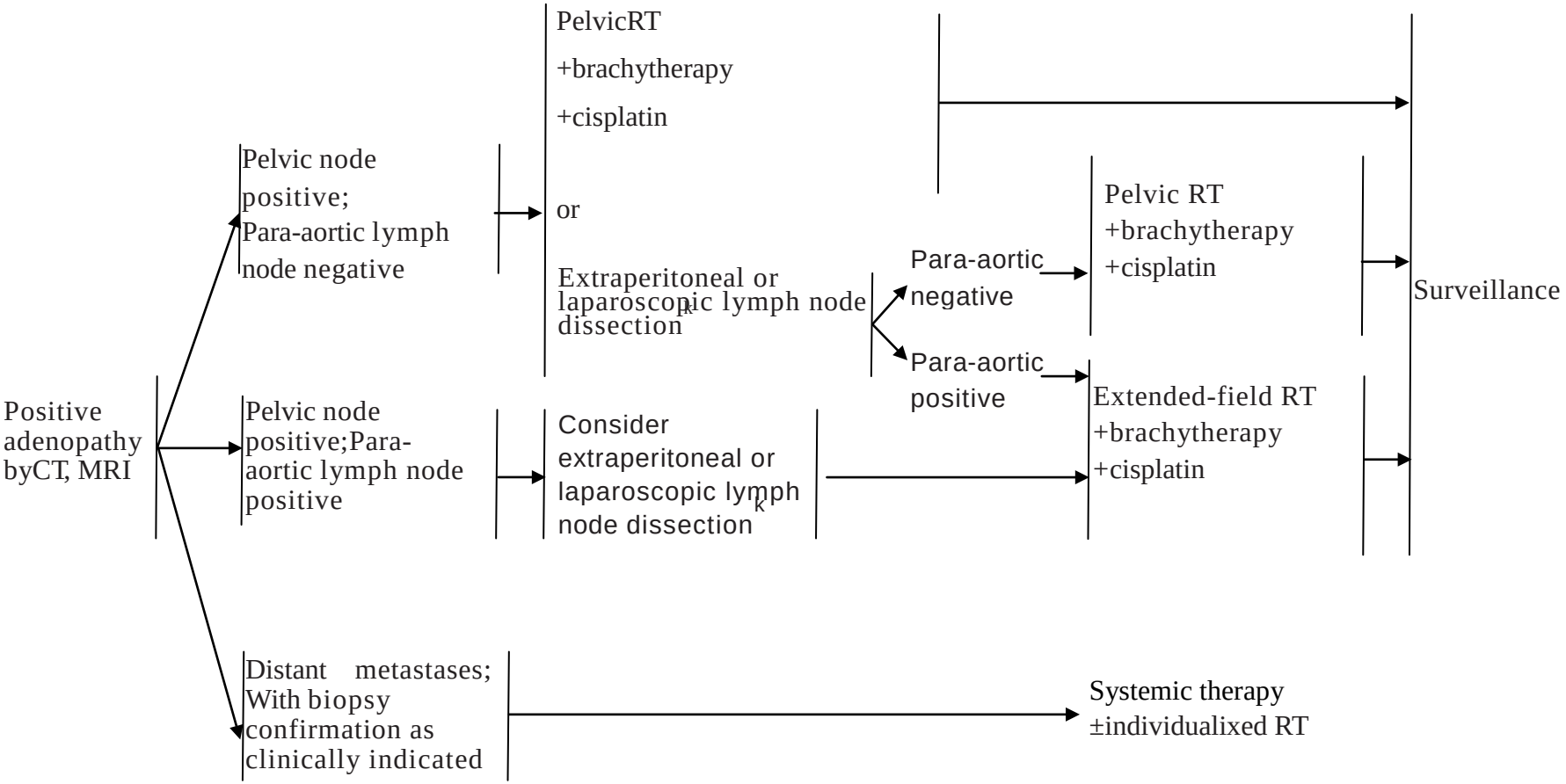
StageIB2,IIA2;StageIIB,IIIA,IIIB,IVA
NODE STATUS

PRIMARY TREATMENT



StageIB2,IIA2
StageIIB,IIIA,IIIB,IVA
IMAGING RESULTS

PRIMARYTREATMENT



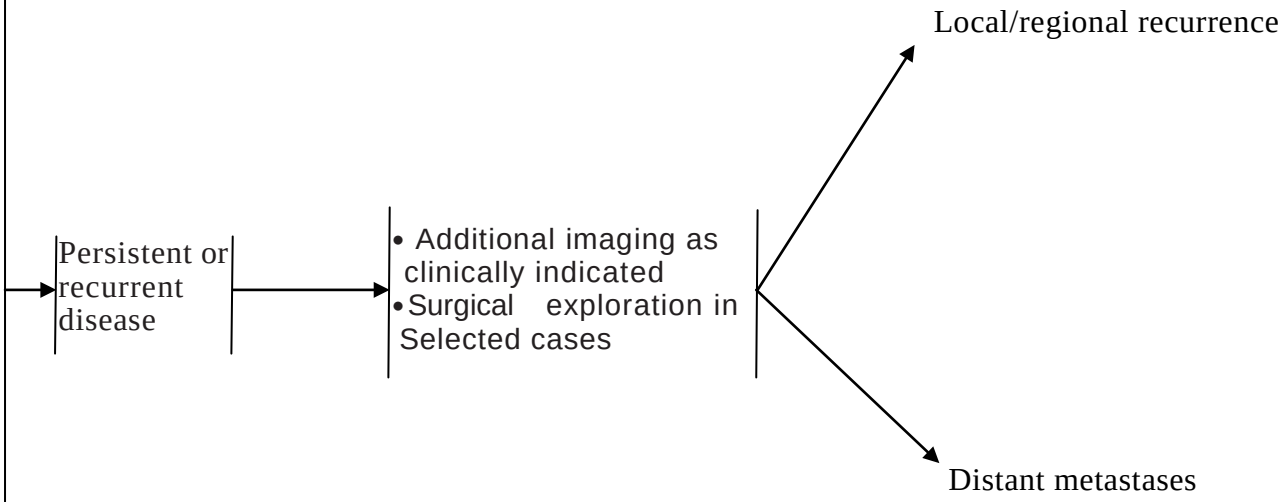
SURVEILLANCE

- Interval History & Physical
- Cervical/vaginalcytology

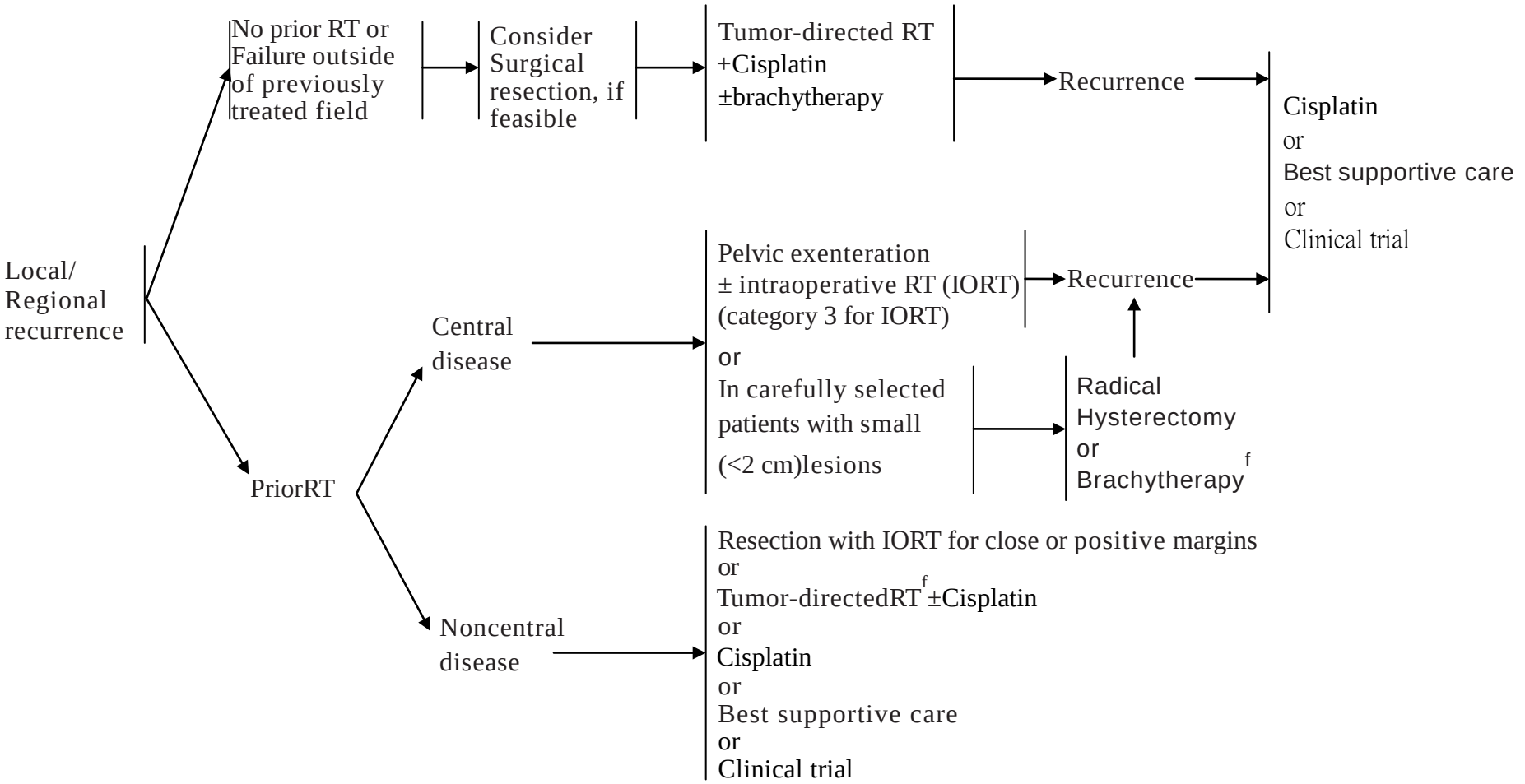
Examination every3-6 mo for2 y,
then every6-12 mo for3-5 y,
then annually(based on patient's risk of disease recurrence).

- Imaging
  - ➢ Chest radiography
  - ➢ CT, MRI,PET-CT Scan as clinically indicated for suspicious recurrence.
- Laboratory assessment
  - ➢ CBC& Platelet
  - ➢ BUN/creatinine findings suspicious for recurrence
- Recommend use of vaginal dilator after RT
- sexual health
- Patient education regarding symptoms, life stytle
- Obesity,exercise

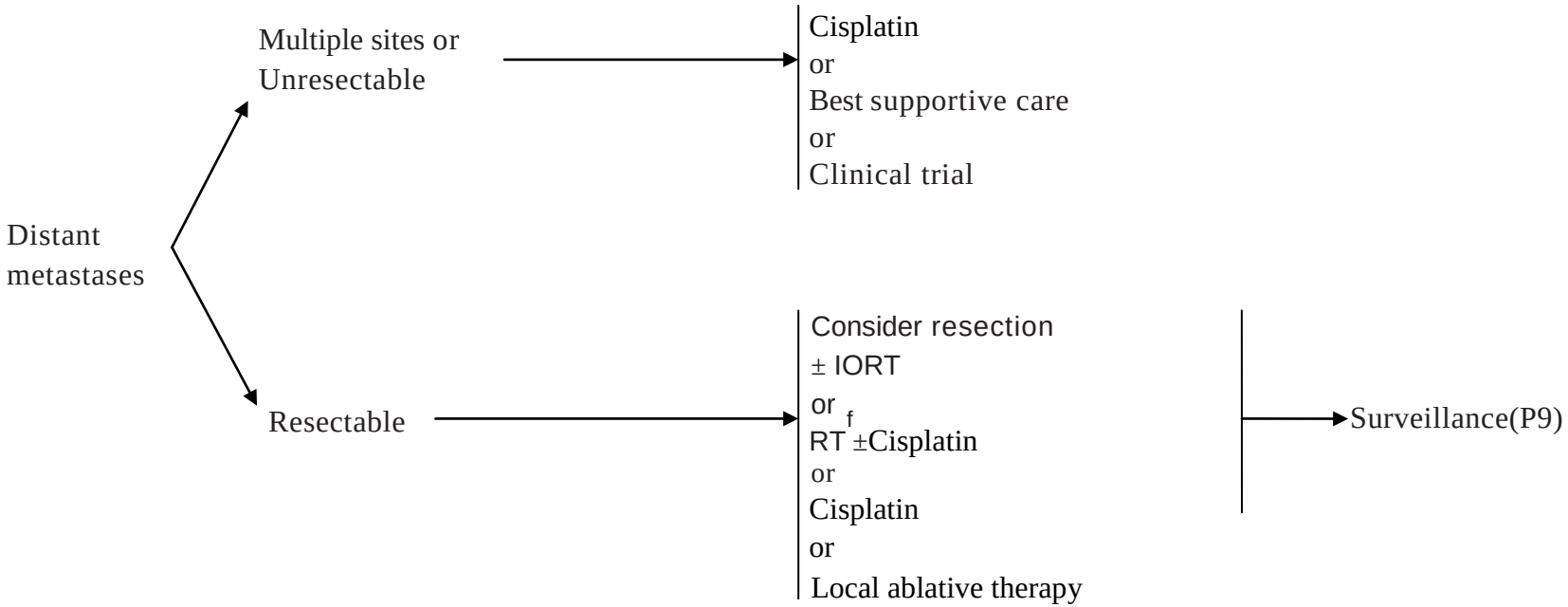
WORKUP



THERAPYFORRELAPSE



THERAPYFOR RELAPSE



一、化學治療

CHEMOTHERAPY REGIMENS FOR RECURRENT OR METASTATIC CERVICAL CANCER†
(Strongly consider clinical trial)

First-line combination therapy
- Cisplatin/paclitaxel+bevacizuma[1]
- Carboplatin/paclitaxel[4,5]
- Cisplatin/topotecan+bevacizumab[6]
- Cisplatin/gemcitabine(category3) [7]
- Cisplatin/paclitaxel(category1) [2,3]

Possible first-line single-agent therapy
- Cisplatin (preferred as a single agent)[3]
- Carboplatin[8]
- Paclitaxel[9]

Second-line therapy
(Agents listed are category 2B unless otherwise noted)
- Bevacizumab
- Docetaxel
- 5-FU (5-fluorouracil)
- Gemcitabine
- Ifosfamide
- Irinotecan
- Mitomycin
- Topotecan
- Pemetrexed
- Vinorelbine

CHEMOTHERAPY REGIMENS FOR RECURRENT OR METASTATIC CERVICAL CANCER

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[5]Kitagawa R, Katsumata N, Shibata T, et al. A randomized, phase III trial of paclitaxel plus carboplatin (TC) versus paclitaxel plus cisplatin (TP) in stage IVb, persistent or recurrent cervical cancer: Japan Clinical Oncology Group study (JCOG0505) [abstract]. J Clin Oncol 2012;30(Suppl 15):Abstract 5006.

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[7]Brewer CA, Blessing JA, Nagourney RA, et al. Cisplatin plus gemcitabine in previously treated squamous cell carcinoma of the cervix. Gynecol Oncol 2006;100:385-388.

[8]Weiss GR, Green S, Hannigan EV, et al. A phase II trial of carboplatin for recurrent or metastatic squamous carcinoma of the uterine cervix: a Southwest Oncology Group study. Gynecol Oncol 1990;39:332-336.

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Ca of cervix : High risk factor:

1.Deep myometrum invasion

2.Tumtor size≧4cm

3.Non-squamous history

4.Parametrium involvement

5.PLN metastasis

二、放射治療政策

(一)　治癒性放射治療(definitive curative radiotherapy alone)：包括全骨盆腔體外放射治療 (whole pelvis external beam radiation therapy) 及局部劑量追加[腔內近接治療(intracavitory radiotherapy, ICRT; intracavitory brachytherapy, ICBT) , 或強度調控放射治療(intensity modulated radiation therapy)。

適應症 (indications)：

1. 早期之子宮頸癌 (IA2, IB1,或 IIA 且腫瘤直徑小於四公分)，不宜或不願手術治療者

2. IB2,或 IIA 且腫瘤直徑大於四公分者(可考慮合併以 cisplatin 為主之化學治療)

3. IIB 以上較晚期之子宮頸癌(可考慮合併以 cisplatin 為主之化學治療)

(二)　術後放射治療(postoperative radiotherapy)：包括全骨盆腔體外放射治療及局部劑量追加[陰道內近接放射治療(intravaginal radiotherapy, IVRT or intravaginal brachytherapy, IVBT), 或強度調控放射治療(intensity modulated radiation therapy。

適應症 (indications)：

早期子宮頸癌 (IA.IB1,或 IIA 腫瘤直徑小四公分者)，手術治療後，病理報告有下列情況者，建議考慮放射治療。

1. 深層基質受侵犯(deep stromal invasion)　2. 淋巴血管受侵犯(lymphvascular invasion)
3. 子宮頸旁組織受侵犯(parametrail invasion) 4. 手術切除邊緣發現癌細胞(positive surgical margin)
5. 骨盆腔淋巴腺轉移(positive pelvic nodes)

(三)　緩解性放射治療: 針對第 IV 期病患之轉移部位(如骨骼、腦等部位)施行緩解性放射治

二、全骨盆腔體外放射治療執行程序**(procedures)**：

(一) 電腦斷層模擬攝影(CT-based simulation)

1. 仰臥、双手置於胸前，並以真空氣墊(vaccum pillow) or alpha cradle 固定姿勢
2. 以雷射光於病人腹部、身體兩側劃上等中心(isocenter)記號
3. 每 3 毫米擷取一張電腦斷層影像
4. 將影像傳送至電腦治療計劃系統(radiation treatment plan, RTP system)

(二) 描繪標靶體積 (contouring target volume)

1. 標靶體積(Gross Target Volume,GTV):電腦斷層或磁振照影影像可量測的病灶(gross lesions seen at CT scan or MRI)
2. 臨床標靶體積(Clinical Target Volume, CTV):
   i. 遠端總腸骨血管(distal common iliac vessels)
   ii. 外腸骨血管(external iliac vessels)
   iii. 內腸骨血管(internal iliac vessels)
   iv. 薦骨前區(presacral region)

(三) Organs At Risk (OAR):

i. 小腸(small bowel)

ii. 直腸(rectum)

iii. 股骨頭(femoral head)

iv. 膀胱(urinary bladder)

(四) 照野邊緣 (border of field)

1. 前後對稱双照野(AP-PA opposed fields):

i. 上緣在第四腰椎與第五腰椎椎椎間處(superiorly at L4-L5 intervertebral space)

ii. 下緣在閉鎖孔下緣或腫瘤遠端下 3 公分處(inferiorly below obturator foramen or 3 cm inferior to distal disease)

iii. 兩側在骨盆邊緣外 1.5-2.0 公分 (bilateraly at 1.5-2.0 cm lateral to pelvc brim)

2. 左右兩側照野(Lateral fields):

i. 前緣在恥骨聯合觸(anteriorly at pubic symphysis)

ii. 後緣在薦骨後方第二薦骨處(posteriorly at S2

(五)　劑量處方 (dose prescription)：

每分次 1.8-2.0 格雷(Gy)，每週五分次，五週總劑量為 45-50 格雷(1.8-2.0 fraction dose,5 fractions per week, total dose 45-50 Gy over 5 weeks)

(六)　劑量限制 (dose constrain):全部體積

1. 小腸：40 Gy
2. 直腸：60 Gy
3. 膀胱:65 Gy
4. 股骨頭:50 Gy

(七)　體外放射治療技術 (external radiotherapy technique)：依病患病情與意願選擇下列技術

1. 傳統四照野全骨盆放射治療 (conventional 4-field whole pelvis radiation therapy)
2. 三維順形放射治療(3-Dimension Conformal Radiation Therapy, 3D-CRT)
3. 強度調控放射治療(Intensity Modulation Radiation Therapy, IMRT)
4. 影像導引放射治療 (Image-guided Radiation Therapy, IGRT)

三、局部劑量追加: 依病患病情與意願選擇下列技術

(一) 腔內近接放射治療 (intracavitory radiotherapy, ICRT or intracavitory brachytherapy, ICBT)

採高劑量率後荷式近接治療(high-dose-rate afterloading brachytherapy)

(二) 單純近接治療 (brachytherapy alone) 可用來治療分期為 IA1 或一些分期為 IA2 的子宮頸癌

(三) 較晚期之子宮頸癌，如 Bulky IB,IIB,IIIA,IIIB 則必需先給予 45-50 Gy/25 fractions/5 weeks 之體外全骨盆放射治療

(四) Point A 劑量

1. 單一近接治療為每分次(fraction) 7 格雷(Gy)，一週二分次，總共七分次.
2. Bulky IB,IIB,IIIA,IIIB 之體外全骨盆放射治療後近接治療為每分次(fraction) 5-6 格雷(Gy)，一週二分次，總共 5-6 分次.

四、陰道內近接放射治療 (intravaginal radiotherapy, IVRT or intravaginal brachytherapy, IVBT)

(一) 適用於手術陰道切除(vaginal cuff)安全邊緣不足或術後放射治療後陰道仍有殘餘腫瘤之病人

(二) 劑量為陰道黏膜下五毫米(5mm)每分次(fraction) 4-5 格雷(Gy)，一週二分次，總共四分次.

五、強度調控放射治療 (intensity modulated radiation therapy)

完成全骨盆放射治療者，計畫標靶體積(planningtarget volume, PTV)應包括 GTV 外加 0.5- 1.0 公分邊界進行局部劑量追加，再給予劑量應為 25-27Gy / 14–15 分次。

六、Concurrent Chemoradiotherapy：External irradiation 49Gr with 29 fraction +Cisplatin 40mg/m^2/wk for 6 weeks.

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1.Monk BJ, Sill MW, McMeekin DS, et al. Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma:A Gynecologic Oncology Group Study. J ClinOncol 2009;27:4649-4655.

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	FIGO	PRIMARY TUMOR (T)
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
Tis	*	Carcinoma in situ (preinvasive carcinoma)
T1	I	Cervical carcinoma confined to uterus (extension to corpus should be disregarded)
T1a**	IA	Invasive carcinoma diagnosed only by microscopy. Stromal invasion with a maximum depth of 5.0 mm measured from the base of the epithelium and a horizontal spread of 7.0 mm or less. Vascular space involvement, venous or lymphatic, does not affect classification
T1a1	IA1	Measured stromal invasion 3.0 mm or less in depth and 7.0 mm or less in horizontal spread
T1a2	IA2	Measured stromal invasion more than 3.0 mm and not more than 5.0 mm with a horizontal spread 7.0 mm or less
T1b	IB	Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a/IA2
T1b1	IB1	Clinically visible lesion 4.0 cm or less in greatest dimension
T1b2	IB2	Clinically visible lesion more than 4.0 cm in greatest dimension
T2	II	Cervical carcinoma invades beyond uterus but not to pelvic wall or to lower third of vagina
T2a	IIA	Tumor without parametrial invasion
T2a1	IIA1	Clinically visible lesion 4.0 cm or less in greatest dimension
T2a2	IIA2	Clinically visible lesion more than 4.0 cm in greatest dimension
T2b	IIB	Tumor with parametrial invasion
T3	III	Tumor extends to pelvic wall and/or involves lower third of vagina, and/or causes hydronephrosis or non-functioning kidney
T3a	IIIA	Tumor involves lower third of vagina, no extension to pelvic wall
T3b	IIIB	Tumor extends to pelvic wall and/or causes hydronephrosis or non-functioning kidney
T4	IVA	Tumor invades mucosa of bladder or rectum, and/or extends beyond true pelvis (bullous edema is not sufficient to classify a tumor as T4)
		*FIGO staging no longer includes Stage 0 (Tis)
		** All macroscopically visible lesions—even with superficial invasion—are T1b/IB

	FIGO	REGIONAL LYMPH NODES (N)
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1	IIIB	Reginal lymph node metastasis
	FIGO	DISTANT METASTASIS (M)
M0		No distant metastasis (no pathologic M0; use clinical M to complete stage group)
M1	IVB	Distant metastasis (including peritoneal spread, involvement of supraclavicular or mediastinal lymph nodes, lung, liver, or bone)

STAGE			
GROUP	T	N	M
Stage 0*	Tis	N0	M0
Stage I	T1	N0	M0
Stage IA	T1a	N0	M0
Stage IA1	T1a1	N0	M0
Stage IA2	T1a2	N0	M0
Stage IB	T1b	N0	M0
Stage IB1	T1b1	N0	M0
Stage IB2	T1b2	N0	M0
Stage II	T2	N0	M0
Stage IIA	T2a	N0	M0
Stage IIA1	T2a1	N0	M0
Stage IIA2	T2a2	N0	M0
Stage IIB	T2b	N0	M0
Stage III	T3	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T3b T1-3	Any N N1	M0 M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1
*FIGO no longer includes Stage 0 (Tis)			
Stage unknown			