中 山 醫 學 大 學 附 設 醫 院

子 宮 頸 侵 襲 癌 診 療 指 引

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臨床指引參考台灣國家衛生研究院、與美國 NCCN 版本
再依據中山醫學大學附設醫院婦癌小組經驗作編修
婦癌醫療小組

癌症委員會主任委員	癌症委員會執行長	癌症中心主任	團隊負責人

修訂內容

頁數	原文	修訂/新增
1	本子宮頸癌診斷及治療指引的建立，除了依據已發表的實證醫學證據及專家意見外，並參考國家衛生研究院子宮頸侵襲癌臨床指引、美國 National Comprehensive Cancer Network (NCCN) 的 Practice Guide-lines in Cervical Cancer 2022,V1版、FIGO Staging Classifications and Clinical Practice Guidelines in the Management of Gynecologic Cancer、及中山醫學大學附設醫院子宮頸癌治療經驗進行編修。	本子宮頸癌診斷及治療指引的建立，除了依據已發表的實證醫學證據及專家意見外，並參考國家衛生研究院子宮頸侵襲癌臨床指引、美國 National Comprehensive Cancer Network (NCCN) 的 Practice Guide-lines in Cervical Cancer 2024,V1版、FIGO Staging Classifications and Clinical Practice Guidelines in the Management of Gynecologic Cancer、及中山醫學大學附設醫院子宮頸癌治療經驗進行編修。
16	Consider ~~interval~~ hysterectomy	Consider **radical** hysterectomy
20	已接受過放射治療者，Central disease 復發且新增 In carefully selected patients with small (<2 cm) lesions	新增Individualized EBRT ± concurrent platinumcontaining chemotherapy
24	新增	Other Recommended Regimens (if cisplatin and carboplatin are unavailable) ・Capecitabine/mitomycin ・Gemcitabine ・Paclitaxel
25	**Squamous Cell Carcinoma,Adenocarcinoma, or Adenosquamous Carcinoma** **Second-line therapy** 增修	Preferred Regimens ・Pembrolizumab (for PD-L1 positive or MSI-H/dMMR tumors/TMB-H tumors) • ~~Nivolumab for PD-L1 positive tumors~~ • Tisotumab vedotin-tftv • Cemiplimab Other Recommended Regimens ・Bevacizumab (Avastin癌思停/MVASI艾法施) ・Paclitaxel ・Albumin-bound paclitaxel ・Docetaxel

		·5-FU(5-fluorouracil) ·Gemcitabine ~~·Ifosfamide~~ ·Irinotecan ~~·Mitomycin~~ ·Pemetrexed ·Topotecan ·Vinorelbine Useful in Certain Circumstances · PD-L1–positive tumors Nivolumab · HER2-positive tumors (IHC 3+ or 2+) Fam-trastuzumab deruxtecan-nxki · RET gene fusion-positive tumors Selpercatinib · NTRK gene fusion-positive tumors Larotrectinib Entrectinib
26	**Small Cell NECC** First-line therapy 新增	Other Recommended Regimens • Cisplatin/etoposide + atezolizumab(or durvalumab) • Carboplatin/etoposide + atezolizumab(or durvalumab) • Topotecan/paclitaxel/bevacizumab • Cisplatin/paclitaxel • Carboplatin/paclitaxel (for patients who have received prior cisplatin therapy)
26	**Small Cell NECC** Second-line therapy 增修	~~See first-line or second-line therapy on「Squamous Cell Carcinoma, Adenocarcinoma, or Adenosquamous Carcinoma」Other Recommended Regimens~~ • Bevacizumab

		• Albumin-bound paclitaxel • Docetaxel • Topotecan • Topotecan/paclitaxel • Cisplatin/topotecan • Cisplatin • Carboplatin • Paclitaxel • Irinotecan **備註：Large cell化學治療處方建議可參照Small Cell NECC辦理。**

目 錄

一、 前言

本共識手冊內所提之各種診治意見，為原則性之建議，希望能為癌症患者及其家屬提供一個正確的指引；但對臨床醫師之醫療行為無絕對之法律性約束力！由於醫藥科技持續在進步，每位患者的病情亦不盡相同；醫師應就病人之病情做個別的考量，病人和家屬亦應與醫師溝通討論，以決定最適當之診治方式。

我國2019年共4507例子宮頸癌新病例，包括侵襲癌症1393例及原位癌3114例。因子宮頸癌死亡人數674人，死亡率每十萬人5.66人，為女性癌症死亡的第八名。根據 2022年衛生署公佈2019年的癌症統計資料，子宮頸癌排名女性第八大癌症死因，在肺癌、乳癌、肝癌、結腸直腸癌、胰臟癌、胃癌以及卵巢癌之後，子宮頸癌死亡年齡中位數為64歲；子宮頸癌死亡人數有9成以上是集中於45歲以上；其死亡率隨年齡增加而遞增。

已開發國家子宮頸癌死亡率的顯著下降，被認為是有效篩檢的結果。高風險性人類乳突病毒 (high risk human papillomavirus, HPV) 的感染是子宮頸癌形成的重要因子。在子宮頸癌發生率高的國家，人類乳突病毒感染的盛行率約10 - 20%，高於低發生率國家的5 - 10%。幾乎所有的子宮頸癌組織中都可以發現高風險性人類乳突病毒的存在，以及不同族群中子宮頸癌發生率和人類乳突病毒感染盛行率之間的正向相關，顯示出二者之間的關聯。其它與子宮頸癌有關的風險因子，包括抽煙、生產次數、口服避孕藥的使用、發生性行為的年齡、性伴侶人數、低社經地位、性病史以及慢性免疫功能缺乏等等。雖然各國侵襲性子宮頸癌的發生率不同，但是診斷及治療的原則大致相同。

本子宮頸癌診斷及治療指引的建立，除了依據已發表的實證醫學證據及專家意見外，並參考國家衛生研究院子宮頸侵襲癌臨床指引、美國 National Comprehensive Cancer Network (NCCN) 的 Practice Guide-lines in Cervical Cancer2024,V1版、FIGO Staging Classifications and Clinical Practice Guidelines in the Management of Gynecologic Cancer、及中山醫學大學附設醫院子宮頸癌治療經驗進行編修。

二、 組織病理分類與分化

鱗狀上皮癌(Squamous cell carcinoma) 佔所有病例的80 - 85%，腺癌(Adeno-carcinoma)及腺鱗狀上皮癌 (Adenosquamous carcinoma)分別佔約15%以及 3 - 5%，其餘亮細胞癌(clear cell carcinoma)、類子宮內膜腺癌(endometrioid adenocarcinoma)、未分化細胞癌(undifferentiated carcinoma)、神經內分泌腫瘤(neuroendocrine tumor)內含小細胞癌(small cell carcinoma)，以及惡性子宮頸肉瘤則更罕見。本指引僅對較為常見之子宮頸癌加以論述。子宮頸癌的病理組織分化分為：

分化良好	**(grade 1)**
分化中度	**(grade 2)**
分化不良或未分化	**(grade 3)**
分化無法評估	**(grade x)**

三、 症狀、診斷和檢查

早期子宮頸癌的症狀包括持續的陰道分泌物、性交後出血或間歇性出血，這些輕微而非特異性的症狀經常為病患忽略，有些侵襲性子宮頸癌甚至沒有症狀。子宮頸抹片則是篩檢子宮頸癌前病變或微侵襲子宮頸癌的方法，並不適用於確認或排除已經高度懷疑是子宮頸癌的病灶。婦產科醫師可以經由目視或陰道鏡檢查直接觀察子宮頸表面是否有型態上的變化；對於可疑的病灶，子宮頸切片是簡單而能得到明確診斷的方法。因此，診斷子宮頸癌最確切的方法是子宮頸切片。假如子宮頸切片不足以確認是否為侵襲癌或是需進一步確定顯微侵襲的可能時，可採用子宮頸錐狀手術。如果子宮頸切片已經確診為侵襲性子宮頸癌，就不應再施行子宮頸錐狀手術。NCCN提到除非有禁忌症，電腦斷層攝影及核磁共振為必要

影像學檢查，重視MRI以評估局部病灶，重視PET /CT以評估全身情況。

如果醫師無法藉由詳細的內診決定兩側子宮頸旁組織是否已經有因癌組織轉移導致的硬結，可使用麻醉下的內診檢查(examination under anesthesia)進一步確定；對於大體積腫瘤和/或腫瘤向前方延展者，藉由膀胱鏡檢查(cystoscopy)並對可疑部位切片，可以確定是否已有膀胱黏膜的侵襲；假如肛診懷疑有直腸侵襲，則可藉由直腸鏡檢查(proctoscopy) 及對可疑部位切片確認。由於子宮頸癌可能導致輸尿管阻塞，必須藉由泌尿道系統的檢查以排除或確定其存在的可能性。可使用靜脈腎盂攝影 (intravenous pyelography, IVP)、腎臟及膀胱超音波 (renal and bladder ultrasonography)、電腦斷層(computed tomography, CT)或核磁共振(magnetic resonance imaging, MRI)；對骨盆器官的侵襲可選擇性使用恥骨上或陰道超音波(supra-pubic or vaginal ultrasonography)或MRI來評估；CT、MRI可選擇性的使用於評估淋巴結的狀況。子宮頸癌的腫瘤指標squamous cell carcinoma antigen (SCC-Ag)或carcinoembryonic antigen (CEA) 對於鱗狀上皮癌，CA125及CEA對於腺細胞癌，可以做為治療前評估腫瘤進展程度的大略參考，治療前腫瘤指標超出正常值的病患，治療後也可以使用該指標評估治療效果及做為追蹤的工具。

四、 分期

子宮頸癌的分期有 FIGO分期(國際婦產科聯盟International Federation of Gynecology and Obstetrics, FIGO) 及**AJCC TNM**分期兩種系統:

FIGO 分期(2018)	
I	The carcinoma is strictlyconfined to the cervix (extension to the uterine corpus should be disregarded)
IA	Invasive carcinoma that can be diagnosed only by microscopy. with maximum depth of invasion≦5mm
IA1	Measured stromal invasion≦3 mm in depth
IA2	Measured stromal invasion >3 mm and ≦ 5mm in depth
IB	Invasive carcinoma with measured deepest invasion > 5mm(greater than Stage IA),lesion limited to the cervix uteri with size measured by maximum tumor diameter
IB1	Invasive carcinoma > 5mm depthof stromal invasion, and ≦ 2cm in greatest dimension
IB2	Invasive carcinoma > 2cm and ≦ 4cm in greatest dimension
IB3	Invasive carcinoma > 4cm in greatest dimension
II	The carcinoma invades beyond the uterus, but has not extended onto the pelvic wall or to lower third of the vagina
IIA	Involvement limited to the upper two-thirds of the vagina without parametrial invasion
IIA1	Invasive carcinoma ≦ 4cm in greatest dimension
IIA2	Invasive carcinoma > 4cm in greatest dimension
IIB	With parametrial involvement but not up to the pelvic wall
III	The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functional kidney and/or involves pelvic and/or para-aortic lymph nodes
IIIA	The carcinoma involves the lower third of vagina,with no extension to pelvic wall.
IIIB	Extends to pelvic wall and/or hydronephrosis or non-functional kidney.(unless know to be due to another cause)
IIIC	Involvement of pelvic and/ or para-aortic lymph nodes(including micrometastases), irrespective of

	tumor size and extent(with r and p notations).
IIIC1	Pelvic lymph node metastasis only
IIIC2	para-aortic lymph node metastasis
IV	The carcinoma has extended beyond the true pelvis or has involved (biopsy proven)the mucosa of the bladder or rectum.(A bullous edema ,as such, dose not permit a case to be allotted to stage IV)
IVA	Spread to adjacent pelvic organs
IVB	Spread to distant organs

TNM 分期(AJCC 9th)

Definition of primary Tumor(T)

T Category	FIGO Stage	T Criteria
Tx		Primary tumor cannot be assessed.
T0		No evidence of primary tumor.
T1	**I**	Carcinoma is strictly confined to the cervix (extension to the corpus should be disregarded)
T1a	**IA**	Invasive carcinoma that can be diagnosed only by microscopy with maximum depth of invasion ≦5 mm
T1a1	**IA1**	Measured stromal invasion≦3 mm in depth
T1a2	**IA2**	Measured stromal invasion >3 mm and ≦5 mm in depth
T1b	**IB**	Invasive carcinoma with measured deepest invasion >5 mm (greater than stage IA); lesions limited to the cervix uteri with size measured by maximum tumor diameter Note:The involvement of vascular/lymphatic spaces should not change then staging.The lateral extent of the lesion is no longer considered.
T1b1	**IB1**	Invasive carcinoma >5 mm depth of stromal invasion and ≦2 cm in greater

		dimension
T1b2	**IB2**	Invasive carcinoma >2 cm and ≦4 cm in greater dimension
T1b3	**IB3**	Invasive carcinoma >4 cm in greater dimension
T2	**II**	Carcinoma invades beyond the uterus, but has not extended on to the lower third of the vagina or to pelvic wall
T2a	**IIA**	Involvement limited to the upper two-thirds of the vagina without parametrial invasion
T2a1	**IIA1**	Invasive carcinoma ≤4 cm in greatest dimension
T2a2	**IIA2**	Invasive carcinoma >4 cm in greatest dimension
T2b	**IIB**	With parametrial invasion but not up to the pelvic wall
T3	**III**	Carcinoma involves lower third of vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney. Note: The pelvic wall is defined as the muscle,fascia,neurovascular structures,and skeletal portions of the bony pelvis.Cases with no cancer-free space between the tumor and pelvic wall by rectal examination are FIGO III.
T3a	**IIIA**	Carcinoma involves lower third of vagina,with no extension to pelvic wall.
T3b	**IIIB**	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney.(unless known to be due to another cause)
T4	**IVA**	Carcinoma has involved(biopsy-proven) the mucosa of the bladder or rectum ,or has spread to adjacent organs.(Bullous edema,as such,dose not permit a case to be assigned to stage IVA)
Definition of Regional Lymph Node(N)		
N Category	**FIGO Stage**	**N Criteria**

NX		Regional lymph nodes cannot be assessed.
N0		No regional lymph nodes metastasis
N0(i+)		Isolated tumor cells in regional lymph node(s)≦0.2 mm, or single cells or clusters of cells ≦200 cells in a single lymph node cross section
N1	**IIIC1**	Regional lymph nodes metastasis to pelvic lymph nodes only
N1mi	**IIIC1**	Regional lymph nodes metastasis(>0.2 mm but ≦2.0 mm in diameter)to pelvic lymph nodes
N1a	**IIIC1**	Regional lymph nodes metastasis(>2.0 mm in diameter) to pelvic lymph nodes
N2	**IIIC2**	Regional lymph nodes metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes
N2mi	**IIIC2**	Regional lymph nodes metastasis(>0.2 mm but ≦2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvic lymph nodes
N2a	**IIIC2**	Regional lymph nodes metastasis(>2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvic lymph nodes
Definition of Distant Metastasis(M)		
M Category	**FIGO Stage**	**M Criteria**
M0		No distant metastasis
cM1	**IVB**	Distant metastasis(includes metastasis to inguinal lymph nodes,intraperitioneal disease, lung, liver, or bone)(excludes metastasis to pelvic or para-aortic lymph nodes,or vagina)
pM1	**IVB**	Microscopic confirmation of distant metastasis(includes metastasis to inguinal lymph nodes,intraperitioneal disease, lung, liver, or bone)(excludes metastasis to pelvic or para-aortic lymph nodes,or vagina)

AJCC PROGNOSTIC STAGE GROUPS

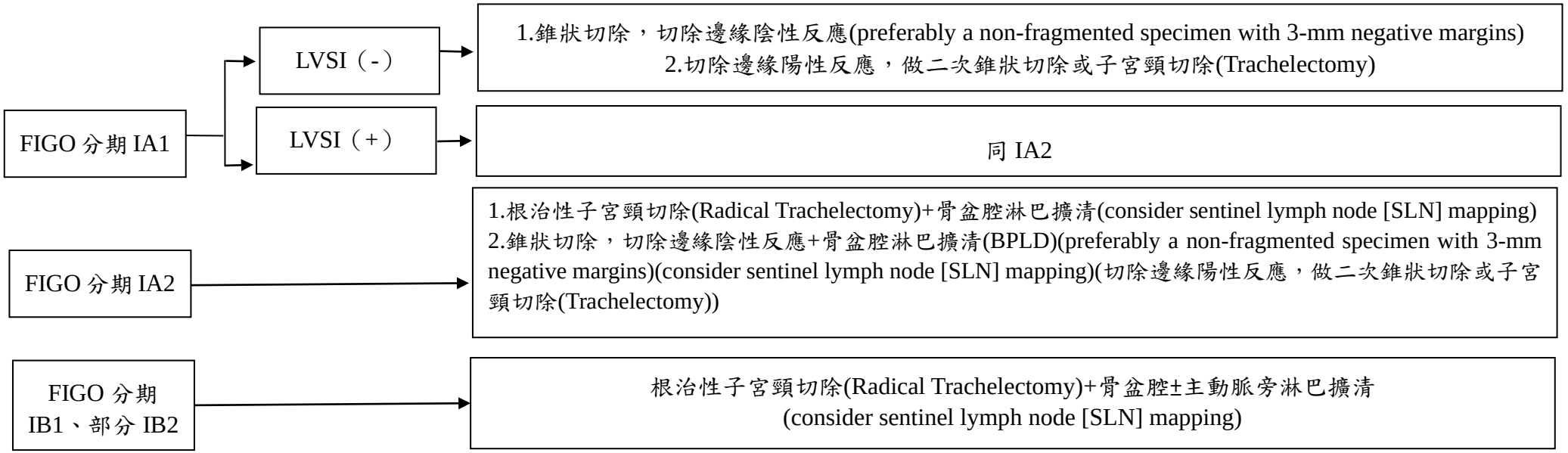
When T is…	And N is…	And M is…	Then the stage group is …
T1	N0	M0	I
T1a	N0	M0	IA
T1a1	N0	M0	IA1
T1a2	N0	M0	IA2
T1b	N0	M0	IB
T1b1	N0	M0	IB1
T1b2	N0	M0	IB2
T1b3	N0	M0	IB3
T2	N0	M0	II
T2a	N0	M0	IIA
T2a1	N0	M0	IIA1
T2a2	N0	M0	IIA2
T2b	N0	M0	IIB
T3	N0	M0	III
T3a	N0	M0	IIIA
T3b	N0	M0	IIIB
TX, T0, T1-3	N1	M0	IIIC1
TX, T0, T1-3	N2	M0	IIIC2
T4	Any N	M0	IVA
Any T	Any N	M1	IVB

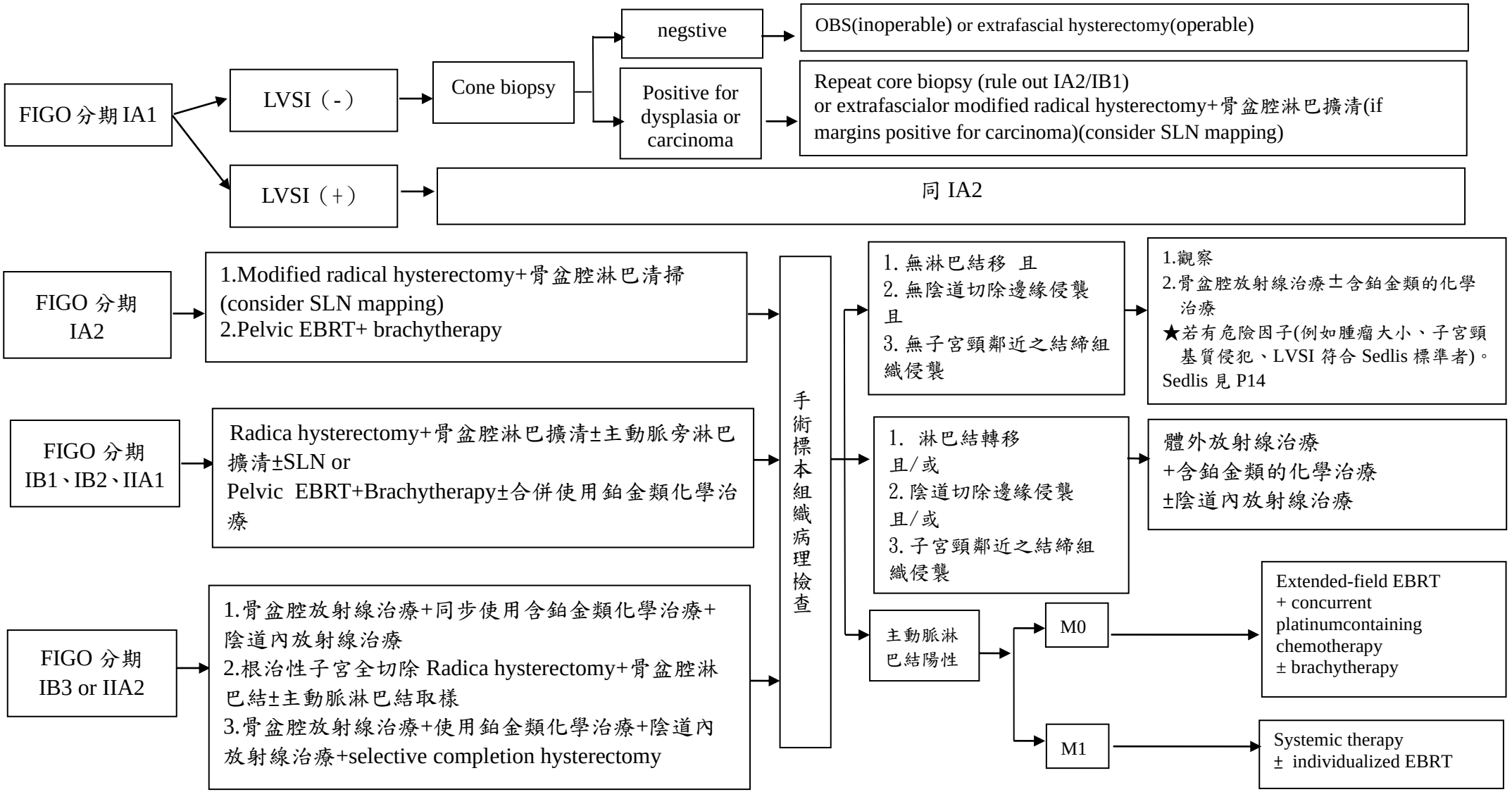
子宮頸癌首次治療臨床指引

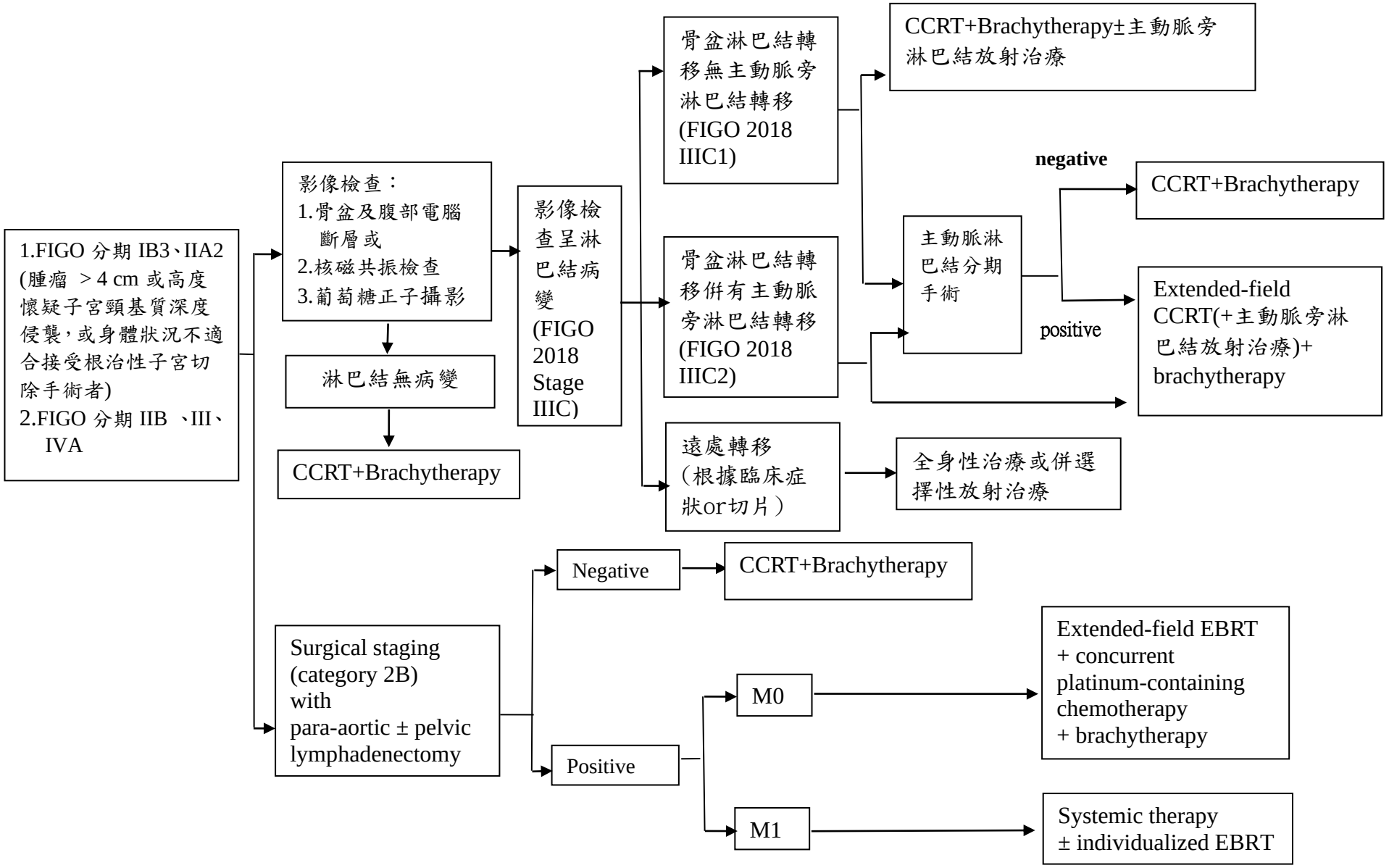
WORK UP

1.病史及理學檢查
2.全血球計數
3.子宮頸切片之組織病理檢查
4.影像學檢查(CXR、MRI/CT、PET)
5.Brain MRI(Opional,for small cell NECC only)
6.膀胱鏡(Opional)
7.直腸鏡(Opional)
8.HIV testing 、HPV testing、tumor markers:CEA、SCC、CA-125(Optional)

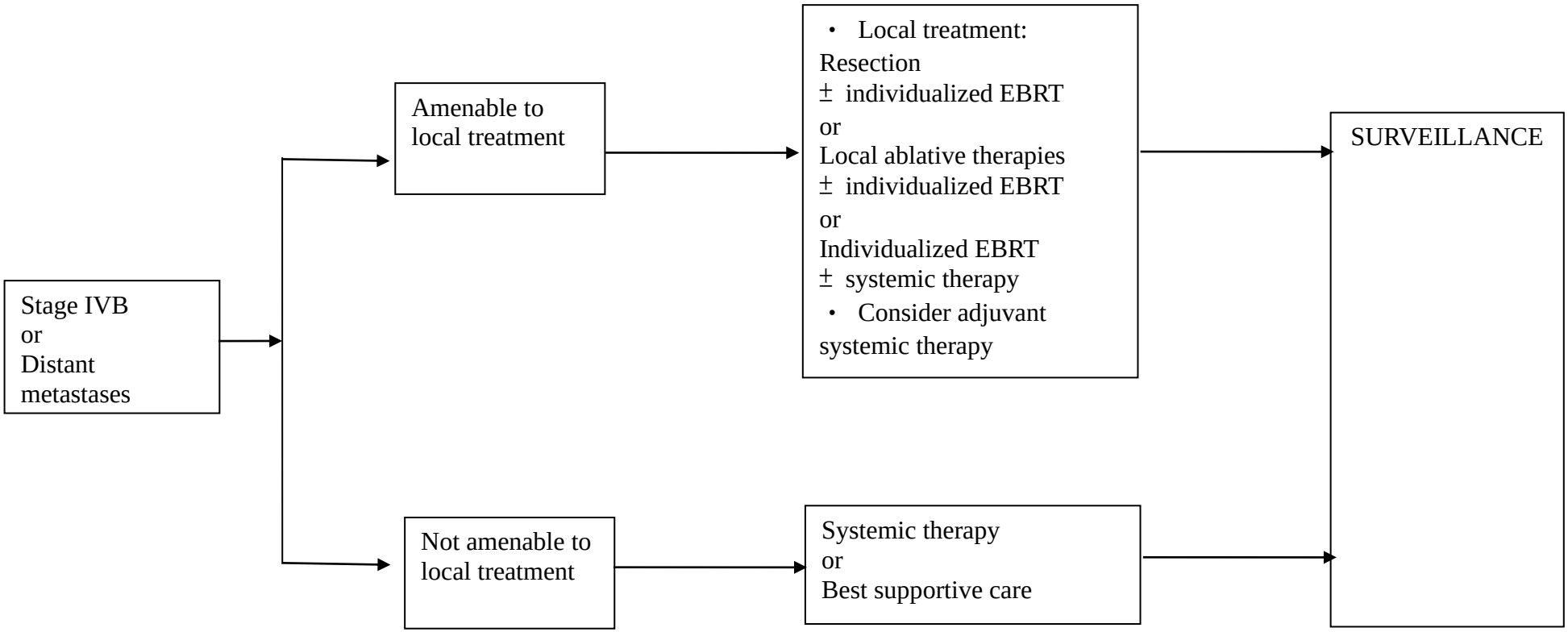
保留生育路徑(Fertility sparing)-適用Stage IA1、IA2、IB1、select IB2




FIGO 分期 IA1
LVSI（-）
Cone biopsy
negstive
OBS(inoperable) or extrafascial hysterectomy(operable)
Positive for dysplasia or carcinoma
Repeat core biopsy (rule out IA2/IB1)
or extrafascialor modified radical hysterectomy+骨盆腔淋巴擴清(if margins positive for carcinoma)(consider SLN mapping)
LVSI（+）
同 IA2
FIGO 分期 IA2
1.Modified radical hysterectomy+骨盆腔淋巴清掃 (consider SLN mapping)
2.Pelvic EBRT+ brachytherapy
FIGO 分期 IB1、IB2、IIA1
Radica hysterectomy+骨盆腔淋巴擴清±主動脈旁淋巴擴清±SLN or
Pelvic EBRT+Brachytherapy±合併使用鉑金類化學治療
FIGO 分期 IB3 or IIA2
1.骨盆腔放射線治療+同步使用含鉑金類化學治療+陰道內放射線治療
2.根治性子宮全切除 Radica hysterectomy+骨盆腔淋巴結±主動脈淋巴結取樣
3.骨盆腔放射線治療+使用鉑金類化學治療+陰道內放射線治療+selective completion hysterectomy
手術標本組織病理檢查
1. 無淋巴結移 且
2. 無陰道切除邊緣侵襲 且
3. 無子宮頸鄰近之結締組織侵襲
1.觀察
2.骨盆腔放射線治療±含鉑金類的化學治療
★若有危險因子(例如腫瘤大小、子宮頸基質侵犯、LVSI 符合 Sedlis 標準者)。
Sedlis 見 P14
1. 淋巴結轉移 且/或
2. 陰道切除邊緣侵襲 且/或
3. 子宮頸鄰近之結締組織侵襲
體外放射線治療
+含鉑金類的化學治療
±陰道內放射線治療
主動脈淋巴結陽性
M0
Extended-field EBRT
+ concurrent platinumcontaining chemotherapy
± brachytherapy
M1
Systemic therapy
± individualized EBRT


1.FIGO 分期 IB3、IIA2 (腫瘤 ＞4 cm 或高度懷疑子宮頸基質深度侵襲，或身體狀況不適合接受根治性子宮切除手術者)
2.FIGO 分期 IIB 、III、IVA
影像檢查：
1.骨盆及腹部電腦斷層或
2.核磁共振檢查
3.葡萄糖正子攝影
淋巴結無病變
CCRT+Brachytherapy
影像檢查呈淋巴結病變 (FIGO 2018 Stage IIIC)
骨盆淋巴結轉移無主動脈旁淋巴結轉移 (FIGO 2018 IIIC1)
骨盆淋巴結轉移併有主動脈旁淋巴結轉移 (FIGO 2018 IIIC2)
遠處轉移（根據臨床症狀or切片）
CCRT+Brachytherapy±主動脈旁淋巴結放射治療
主動脈淋巴結分期手術
negative
CCRT+Brachytherapy
positive
Extended-field CCRT(+主動脈旁淋巴結放射治療)+ brachytherapy
全身性治療或併選擇性放射治療
Surgical staging (category 2B) with para-aortic ± pelvic lymphadenectomy
Negative
CCRT+Brachytherapy
Positive
M0
Extended-field EBRT + concurrent platinum-containing chemotherapy + brachytherapy
M1
Systemic therapy ± individualized EBRT

TREATMENT


Stage IVB
or
Distant
metastases
Amenable to
local treatment
Not amenable to
local treatment
• Local treatment:
Resection
± individualized EBRT
or
Local ablative therapies
± individualized EBRT
or
Individualized EBRT
± systemic therapy
• Consider adjuvant
systemic therapy
Systemic therapy
or
Best supportive care
SURVEILLANCE

六、根治性手術後的輔助治療

根治性子宮切除手術標本的組織病理檢查如果呈現**高度**風險:包括手術子宮旁或陰道邊緣陽性、淋巴結轉移，病患的預後明顯較差，應接受術後輔助治療。

即使病理檢查沒有呈現淋巴結轉移、腫瘤組織未侵襲達子宮頸旁組織，但有下列因素包括：LVSI positive、子宮基質侵犯深度、主要腫瘤大小(依據臨床觸診)等**中度**危險因子時，仍建議加作CCRT。

SEDLIS CRITERIA: ELIGIBILITY FOR CONSIDERING EXTERNAL PELVIC RADIATION AFTER RADICAL HYSTERECTOMY IN NODE-NEGATIVE. MARGIN-NEGATIVE.PARAMETRIA-NEGATIVE.

LVSI	Stromal invasion	Tumor size(cm) (Determined by clinical palpation)
+	Deep 1/3	Any
+	Middle 1/3	≧2
+	Superficial 1/3	≧5
-	Middle or Deep 1/3	≧4

LVSI: Lymphovascular space invasion

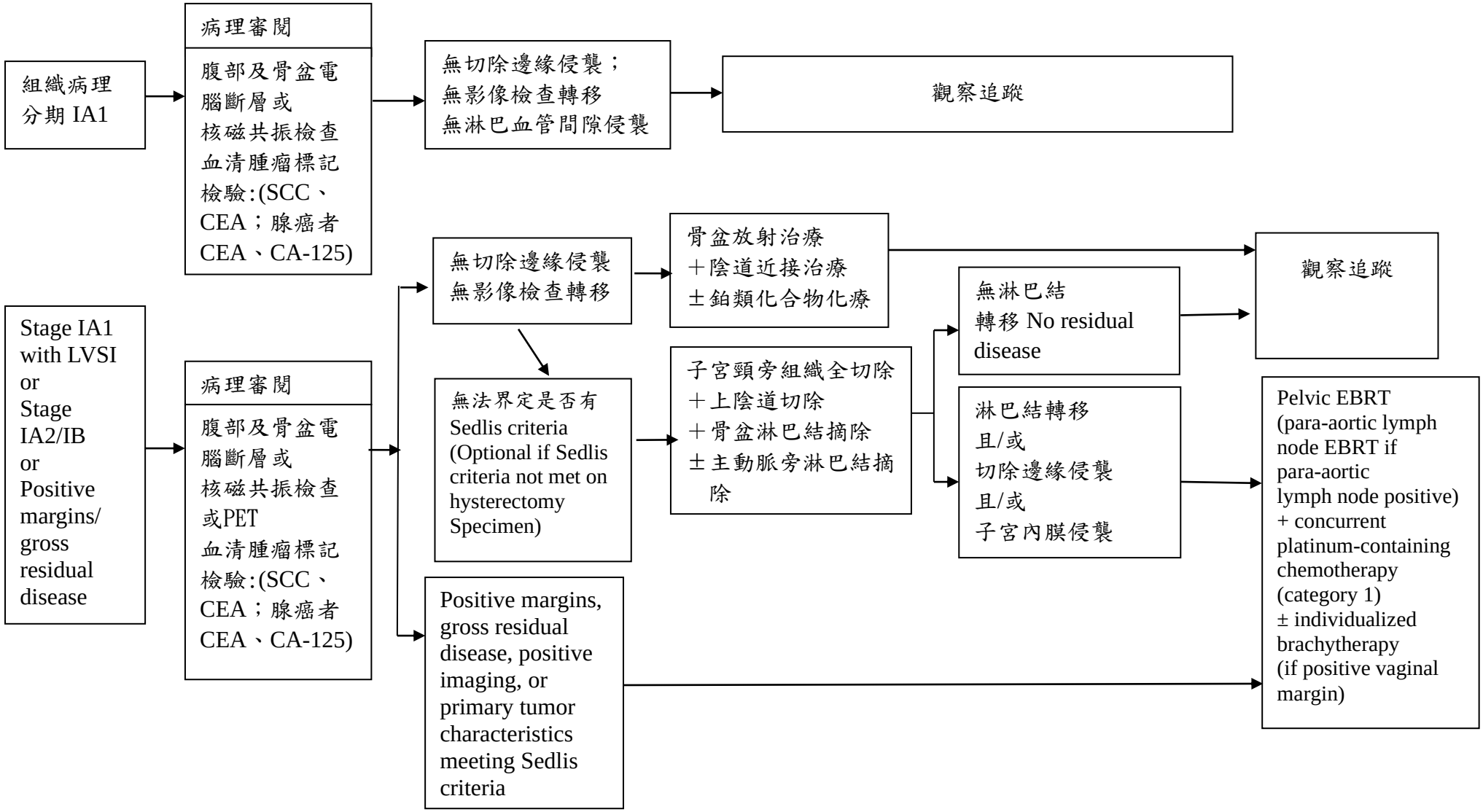
本院臨床指引建議

1、高風險因子個案應給予術後輔助治療 (Pelvic EBRT + concurrent cisplatin containing chemotherapy) 。
2、中度風險因子個案，可以再就手術的範圍，決定安排術後Adjuvant CCRT。
3、超過60歲的高齡婦女，輔助性治療可選擇CCRT或RT alone。
4、60歲以下的婦女，輔助性治療應以CCRT為首選。

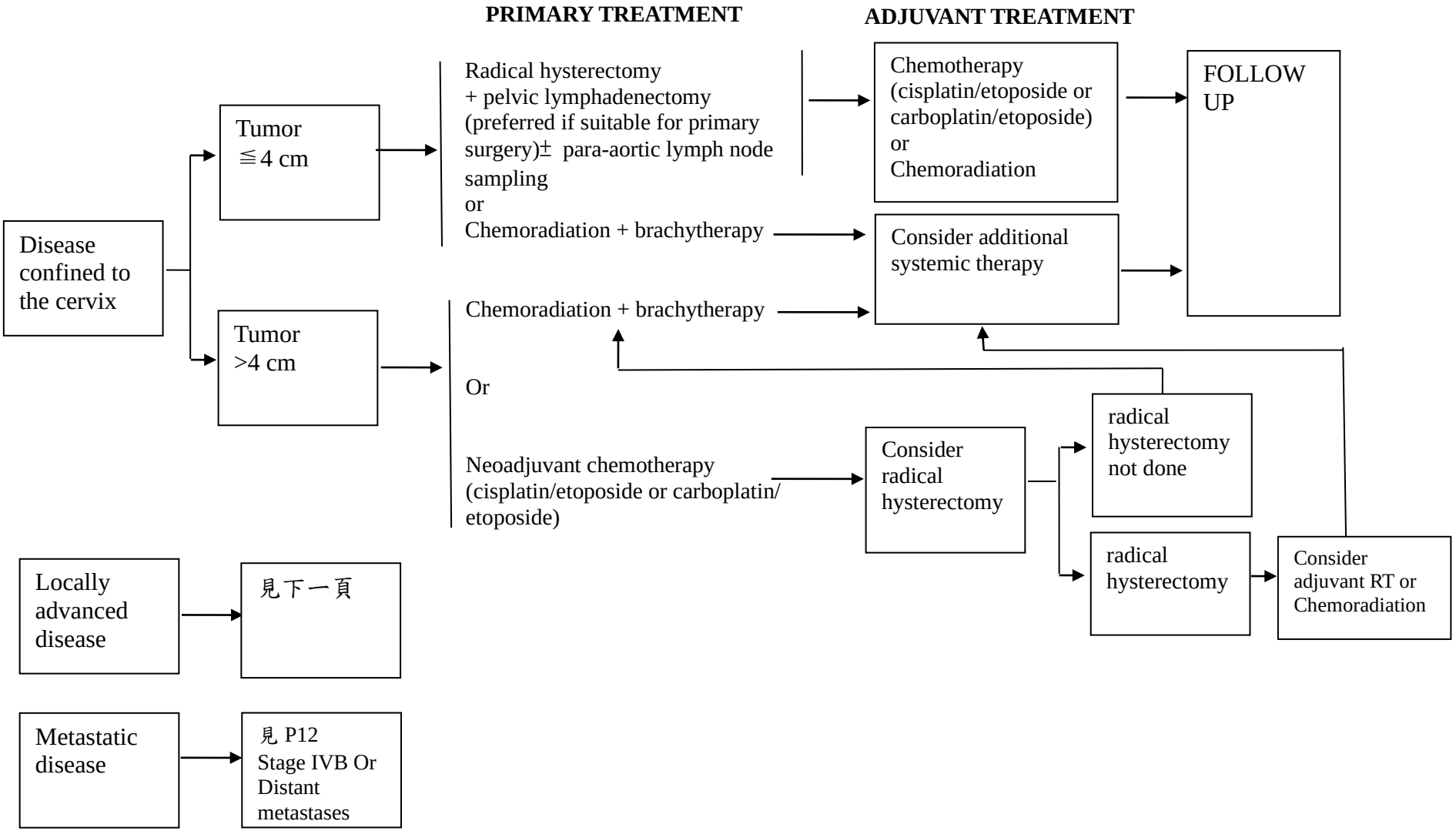
七、單純式子宮切除後意外發現有子宮頸侵襲癌

單純式子宮切除而意外發現有侵襲癌 (FIGO分期為IA1+LVSI或IA2/IB+margin(+)/residucal tumor)時，治療方式應視手術標本邊緣是否有腫瘤組織侵襲決定。若有腫瘤組織侵襲，建議施行CCRT和陰道近接治療；如果沒有腫瘤組織侵襲，可選擇放射治療或子宮頸旁組織全切除(complete parametrectomy)及淋巴結摘除，並切除適當範圍的上段陰道。如果第二次手術的病理檢查發現淋巴結、子宮頸旁組織及陰道邊緣皆無殘留腫瘤組織，可以不需輔助治療。假如淋巴結、子宮頸旁組織或陰道標本邊緣有腫瘤組織侵襲，建議依據上述，給予同時合併含鉑金類化學治療及放射治療。

單純式子宮切除後意外發現有子宮頸侵襲癌臨床指引

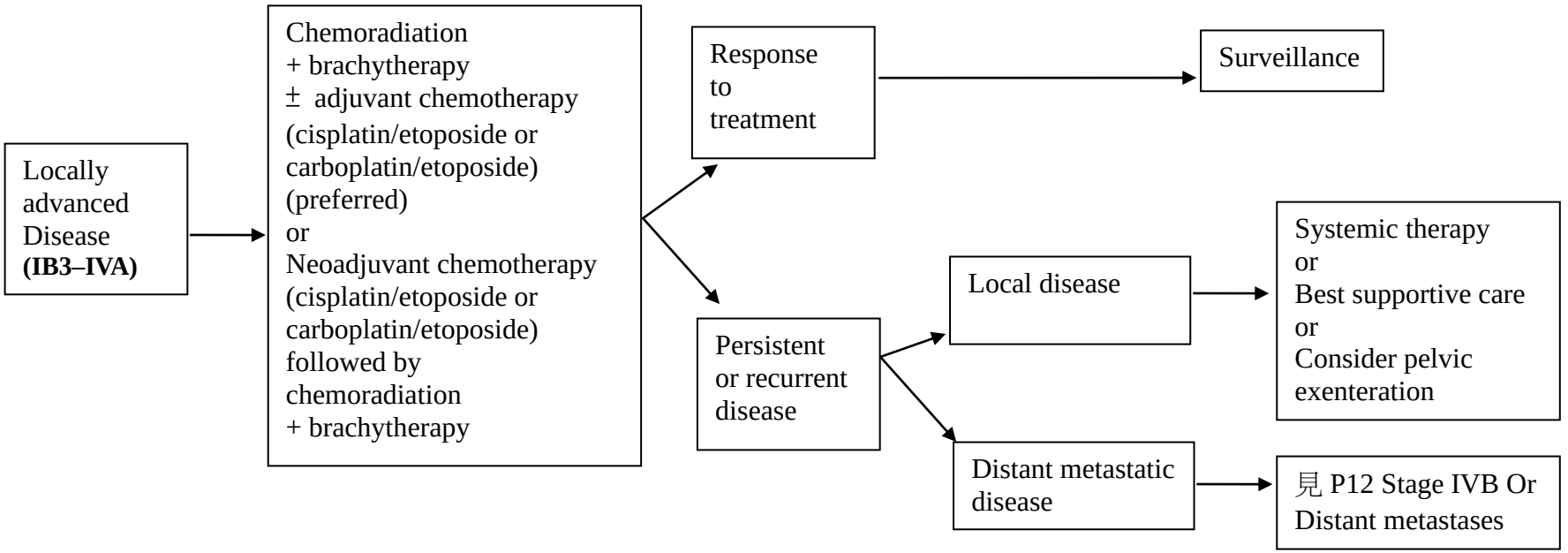


八、SMALL CELL NECC



SMALL CELL NECC(續)

PRIMARY TREATMENT **ADJUVANT TREATMENT**



九、標靶治療

標靶治療藥物-Bevacizumab(癌思停 Avastin/艾法施 MVASI)可用於子宮頸癌合併化療的輔助性治療，包括：初次治療後 CCRT 的合併輔助治療；亦可用於復發後的接續治療或緩和治療。

十、新輔助化學治療(Neo-adjuvant chemotherapy)

針對 Local advanced 的子宮頸癌病人，尤其是年輕個案，可採用新輔助化療 3-6 次後，接續做子宮根除手術與 BPLD。

十一、治療後的追蹤

子宮頸癌完全治療後的追蹤檢查，包括身體狀況的詢問、理學檢查 (包括詳細的骨盆內診) 以及：

1. 抹片檢查：前兩年每3-6個月一次抹片檢查，第三至五年每6-12個月一次，以後每年一次。
2. 血清 SCC-Ag、CEA、CA-125 等腫瘤標記之定期追蹤。
3. 可依病人情況決定是否每6個月全血球計數 (CBC) 、血清腎功能標記 (BUN, creatinine) 檢驗及CTC。
4. 每年可給予胸部 X 光檢查、IVP或腎臟超音波檢查
5. 有臨床適應症時可安排電腦斷層檢查或葡萄糖正子攝影。

十二、復發或持續性疾病的治療 (Salvage Therapy)

子宮頸癌完全治療後，一但發現有復發情形，除非只是陰道的上皮內病變，否則皆應先安排充分的檢查，包括詳細的理學及影像學檢查，如全身電腦斷層檢查或胸部 X光及腹部及骨盆電腦斷層檢查或核磁共振檢查、腫瘤標記檢驗等，以了解全般情況。如果可能，也應選取代表性的可疑病灶，進行切片或細針抽吸取樣，以確定復發。如果懷疑復發的部位僅侷限於單側肺部，而並無主動脈旁淋巴結腫大的情形，必須盡可能排除原發性肺癌的可能性。

經由詳細的檢查以確定復發的範圍後，才能決定治療的方向是以治癒為目標，抑或以減輕不適症狀為目標。原則上，未曾接受放射治療的復發病灶，除了陰道的上皮內病變外，可以施予同時合併放射線及化學治療。單獨的肺、肝或淋巴結轉移可能會因手術切除而有所助益。位於曾經接受過放射治療範圍內的復發病灶，由於其週邊正常組織可以再接受的放射線劑量有限，而此等病灶對於化學治療的反應不佳，需考慮手術的可行性。

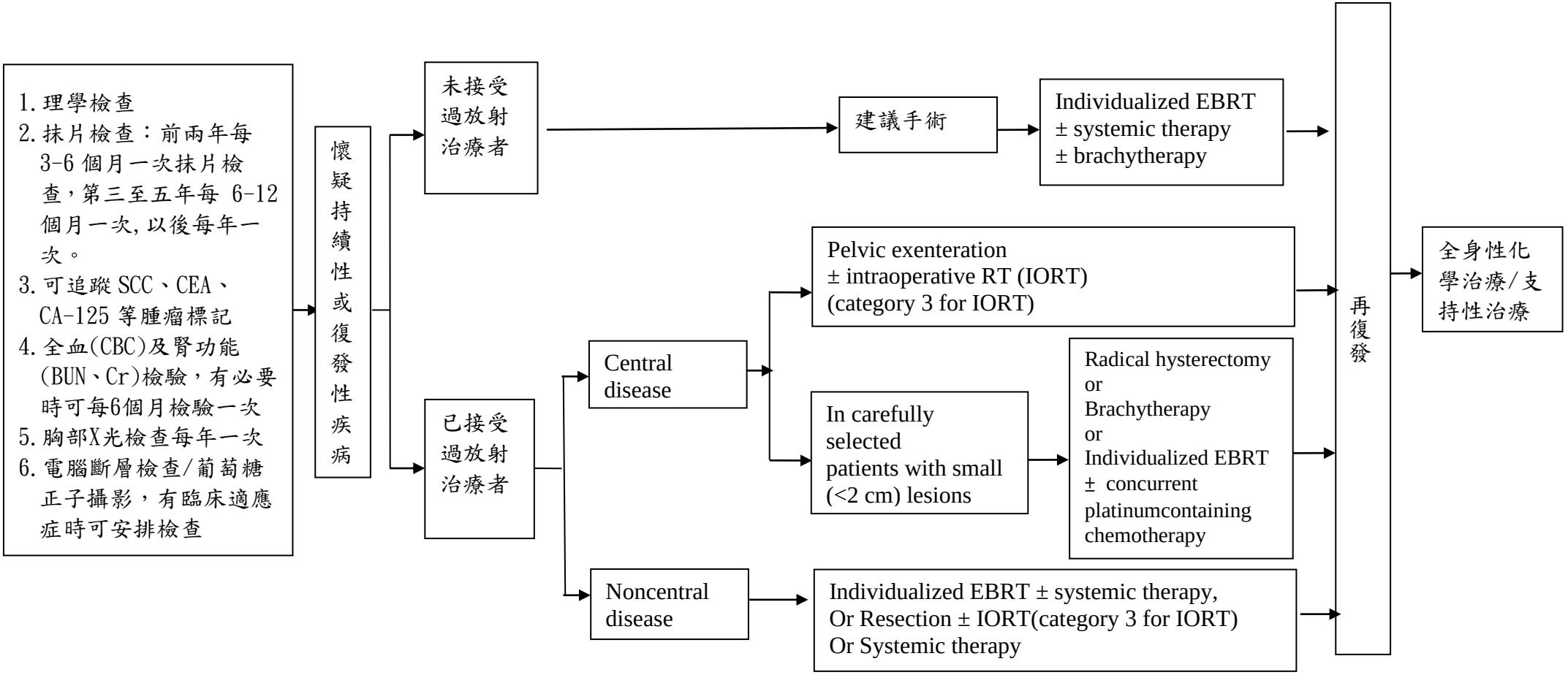
在針對復發或轉移性子宮頸癌上，使用的第一線化學治療藥物有 cisplatin、carboplatin、paclitaxel 、topotecan和Oncovine；而可能使用的第一線合併化學藥物治療有cisplatin / paclitaxel、cisplatin / topotecan、cisplatin / ifosfamide、carboplatin / paclitaxel、cisplatin /Oncovine。

緩和治療：Cisplatin被認為是緩和治療最有效的藥物，其它可以使用的藥物包括ifosfamide、epirubicin、vinorelbine和Taxol。由於緩和治療的目的在於減緩疾病的惡化或減輕因疾病引起的不適，治療時也需考慮維持病患的生活品質，採用單一化學藥物治療是合理的方式，然而合併兩種以上化學藥物治療可能得到較高的腫瘤反應率 (response rate)。生物分子治療和疫苗治療的效果在現階段還沒有確定。

對於全身性治療無效的病人，應視個別情況給予最佳的支持療法，包括臨終照護（hospice care）、疼痛照會、情緒及精神上的支持。

子宮頸癌治療後追蹤及復發的處置臨床指引

定期追蹤方法 **進一步檢查** **救援性（Salvage）治療**



十三、放射治療的使用

放射治療的劑量，除參考標準劑量外，必須將其他因素，如治療範圍、照射方法、正常組織的忍受限度等納入考量。整體的治療時間過度延長，也可能影響治療的效果。部分的回溯性分析發現治療時間超過6至8週以上，每多一天的治療延長，降低0.5 - 1%的骨盆控制率。即使缺乏前瞻性隨機試驗的證實，臨床上仍傾向於在病人情況容許的範圍內，儘量8週內完成全部放射治療療程，而儘量減少延遲或分段放射治療的機會。藉由腹部及骨盆電腦斷層或核磁共振影像的輔助，描繪出腫瘤體積及淋巴結狀態，可以為病人訂定更適當的治療計畫，尤以對於腫瘤體積較大或局部晚期者為然。

十四、放射治療的範圍

在外部照射時使用前後左右四個照野，劑量分佈的規劃宜採用電腦三度空間計算，以確保每個空間的照野都能涵蓋腫瘤，使其可以接受足夠的劑量，而儘量減少正常組織的照射。訂定照野範圍時應考慮腫瘤可能擴散的方向，其前緣應包括至子宮體，後緣應包括子宮薦骨韌帶及薦骨前淋巴結，側緣需要足夠地包涵骨盆淋巴結。**(Level of Evidence 2A, Grade of Recommendation B)**

若是腫瘤侵襲達陰道的下端1/3，需考慮是否將鼠膝部淋巴結納入照射的範圍中。使用延展範圍(extended field)照射主動脈旁淋巴結時需要小心規劃，以確保淋巴結可以接受足夠的劑量(例如以 45 Gy 以治療顯微性疾病)而不超過小腸、脊髓或腎臟的容忍限度。腔內 (intracavitary) 或組織間 (interstitial) 近接治療的安排，除在非常早期的腫瘤外，應於至少施行 40 Gy 的全骨盆體外照射，將腫瘤縮小至近接治療可達成的範圍後才開始進行。**(Level of Evidence 2A, Grade of Recommendation B)**

在大範圍照射後，開始縮小照射範圍，加強照射 (cone down boost) 骨盆淋巴結及子宮頸旁組織時，可藉由中央遮蔽技術降低正常周邊器官(如小腸、直腸和膀胱)接受的放射劑量。子宮頸旁組織及其附近淋

巴結的標準治療總劑量為 60 至65 Gy。
(Level of Evidence 5, Grade of Recommendation D)
(Int J Radiat Oncol Biol Phys. 1997 Jan 1;37(1):237-42)

法國 Institut Gustave-Roussy 於1977 - 1981年間曾以隨機分配方式，對 441位於淋巴攝影顯示或經由病理檢查確定有骨盆淋巴轉移的 FIGO 分期I- IIB病患、或FIGO分期III病患，比較全骨盆或全骨盆合併主動脈旁淋巴結照射的治療效果，結果發現，雖然僅接受骨盆照射組其後發生主動脈旁淋巴結復發的機會較高，然而兩組的局部及遠端復發的機會以及總體存活並無差異。接受合併治療組有較高的機會發生重度腸道併發症。美國放射腫瘤研究組織 (Radiation Therapy Oncology Group, RTOG) 於1979-1986年間，以分層(stratification)隨機分配方式對 367 位子宮頸腫瘤橫(transverse)徑不小於4公分的FIGO分期IB或IIA患者或分期 IIB者，施行全骨盆或全骨盆合併主動脈旁淋巴結照射 (RTOG 79-20)。結果顯示，接受全骨盆合併主動脈旁淋巴結照射組的十年總體存活率為 55%，相較於接受全骨盆照射組的44%，呈顯著差異。兩組的局部復發率相當，而合併主動脈旁淋巴結照射組的遠端首次復發機會較低。兩組的十年無病存活率分別為42%(合併組) 及40% (骨盆照射組)，並無顯著差異。進一步分析發現合併組的局部復發者，治療後有較長的存活率 (25% 對 8%)。其後 RTOG 90-01 [13] 則發現對於IIB - IVA、或 IB - IIA 且腫瘤 5 cm、或經切片證實有骨盆淋巴結轉移但無遠端或主動脈旁淋巴結轉移者，同時合併放射及化學治療的總體存活率顯著提高。然而對於已有主動脈旁淋巴結轉移者，除了化學治療外，如果也計畫給予放射治療，其治療範圍是否應涵蓋主動脈旁淋巴結，仍未有明確的證據。
(Level of Evidence A, Grade of Recommendation B)

我國各醫院皆使用高劑量速率腔內放射系統，一般分成 3 - 6 次治療，每次劑量為 4 - 10 Gy。對於預定接受子宮切除的病人，需要考慮腔內放射劑量的調整。

Principles of Definitive RT

Indications (Clinical Stage)	Target area and dose prescription	LDR equivalent dose
IA2	External beam : Pelvic irradiation to 45~50Gy ICBT : 4.5-6 Gy x 4-6 Fractions	Point A: 75~80Gy
IB1& IIA1 (tumor < 4cm)	External beam : Pelvic irradiation to 45~55Gy ICBT : 4.5-6 Gy x 5-6 Fractions	Point A: 80~85Gy
IB2& IIA2 (tumor > 4cm)	External beam : Pelvic irradiation to 50~60Gy ICBT : 5-6 Gy x 5-6 Fractions	Point A ≧ 85Gy
≧ IIB	External beam : Pelvic irradiation to 50~60Gy ICBT : 5-6 Gy x 5-6 Fractions	Point A ≧ 85Gy

ICBT: intracavitary brachytherapy
LDR: low-dose rate

*If gross disease in the lymph node(+)：Target dose for nodes can range from 54 to 66 Gy

Principles of Neoadjuvant RT

Indications	Target area and dose prescription
Bulky cervical tumor	External beam : Pelvic irradiation to 45~50Gy ± ICBT : 4.5-6Gy x 2-3 Fractions

Principles of Adjuvant RT (after definitive surgery)

Indications (Pathological Stage)	Target area and dose prescription
pN+ and/or positive surgical and/or positive parametrium	External beam : Pelvic irradiation to 45~50Gy Boost the gross residual tumor up to 60~66 Gy IVBT : 4.5-6 Gy x 3-4 Fractions
pN0 if combination of high risk factors (large primary tumor , deep stromal invasion, and lymphovascular invasion)	External beam[a] : Pelvic irradiation to 45~50Gy IVBT : 4.5-6 Gy x 3-4 Fractions

IVBT: intravaginal brachytherapy

1. External beam：IMRT preferred
2. All brachytherapy：HDR(high dose rate)

十五、化學治療

Squamous Cell Carcinoma, Adenocarcinoma, or Adenosquamous Carcinoma

Chemoradiation

preferred regimens
- Cisplatin
- Carboplatin if patient is cisplatin intolerant

Other Recommended Regimens (if cisplatin and carboplatin are unavailable)
- Capecitabine/mitomycin
- Gemcitabine
- Paclitaxel

Recurrent or Metastatic Disease

First-line combination therapy	Possible first-line single agent therapy	Second-line therapy
Preferred Regimens ・Cisplatin/paclitaxel/Bevacizumab (category 1) ・Carboplatin/paclitaxel/Bevacizumab ・ Pembrolizumab(自費) + cisplatin/paclitaxel ± bevacizumab for PD-L1 – positive tumors (category 1) ・ Pembrolizumab(自費) + carboplatin/paclitaxel±bevacizumab for PD-L1 – positive tumors (category 1) Other Recommended Regimens ・Cisplatin / paclitaxel(category 1) ・Carboplatin / paclitaxel	Preferred Regimens ・Cisplatin Other Recommended Regimens ・Carboplatin ・Paclitaxel ・Lipodox	Preferred Regimens ・Pembrolizumab (for PD-L1 positive or MSI-H/dMMR tumors/TMB-H tumors) • Tisotumab vedotin-tftv • Cemiplimab Other Recommended Regimens ・Bevacizumab (Avastin癌思停/MVASI艾法施) ・Paclitaxel ・Albumin-bound paclitaxel ・Docetaxel ・5-FU(5-fluorouracil) ・Gemcitabine ・Irinotecan

(Category 1 for patients who have received prior cisplatin therapy) ・Topotecan/paclitaxel/Bevacizumab (category 1) ・Cisplatin / topotecan ・Topotecan/paclitaxel ・Cisplatin / Oncovine		・Pemetrexed ・Topotecan ・Vinorelbine <u>Useful in Certain Circumstances</u> ・ PD-L1–positive tumors Nivolumab ・ HER2-positive tumors (IHC 3+ or 2+) Fam-trastuzumab deruxtecan-nxki ・ RET gene fusion-positive tumors Selpercatinib ・ NTRK gene fusion-positive tumors Larotrectinib Entrectinib

十五、化學治療(續)

Small Cell NECC

Chemoradiation (preferred regimens) • Cisplatin + etoposide • Carboplatin + etoposide if patient is cisplatin intolerant	
Neoadjuvant Therapy, Adjuvant Therapy, Recurrent or Metastatic Disease	
First-line therapy	**Second-line therapy**
<u>Preferred Regimens</u> ・Cisplatin + etoposide ・Carboplatin + etoposide if patient is cisplatin intolerant <u>Other Recommended Regimens</u>	• Bevacizumab • Albumin-bound paclitaxel • Docetaxel • Topotecan • Topotecan/paclitaxel

• Cisplatin/etoposide + atezolizumab(or durvalumab) • Carboplatin/etoposide + atezolizumab(or durvalumab) • Topotecan/paclitaxel/bevacizumab • Cisplatin/paclitaxel • Carboplatin/paclitaxel (for patients who have received prior cisplatin therapy)	• Cisplatin/topotecan • Cisplatin • Carboplatin • Paclitaxel • Irinotecan

備註：Large cell 化學治療處方建議可參照 Small Cell NECC 辦理。

Adjuvant AND Neoadjuvant chemotherapy

Cisplatin

Cisplatin	40-50mg/m2	iv	d1
wk x 6wks			

Moore DH, Blessing JA, McQuellon RP, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2004;22:3113-3119.

Carboplatin

Carboplatin	AUC (4-6)	iv	d1
wk x 6wks			

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.

Paclitaxel(自費)

Paclitaxel	50- 80mg/m^2	iv	d1
wk x 6 cycles			

Kudelka AP, Winn R, Edwards CL, et al. An update of a phase II study of paclitaxel in advanced or recurrent squamous cell cancer of the cervix. Anticancer Drugs 1997;8:657-661.

Paclitaxel(自費)

Paclitaxel	135-175mg/m^2	iv	d1
Q3W			

Kudelka AP, Winn R, Edwards CL, et al. An update of a phase II study of paclitaxel in advanced or recurrent squamous cell cancer of the cervix. Anticancer Drugs 1997;8:657-661.

Cisplatin +Paclitaxel(自費)

Cisplatin	40-50mg/m^2 iv	d1	
Paclitaxel	50-80mg/m^2 iv	d1	
wk			

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 Clin Oncol 2009;27:4649-4655.
2.Moore DH, Blessing JA, McQuellon RP, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2004;22:3113-3119.

Carboplatin+Paclitaxel (自費)

Carboplatin	AUC (4-6) iv	d1	
Paclitaxel	50- 80mg/m^2 iv	d1	
wk			

Moore KN, Herzog TJ, Lewin S, et al. A comparison of cisplatin/paclitaxel and carboplatin/paclitaxel in stage IVB, recurrent or persistent cervical cancer. Gynecol Oncol 2007;105:299-303.

Cisplatin+Taxol

Cisplatin	75-100mg/m^2 iv		
d1			
Taxol	(135-175)mg/m^2 iv	d1	
q3w			

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 Clin Oncol 2009;27:4649-4655.
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Carboplatin+Taxol

Carboplatin	AUC (4-6) iv	d1	
Taxol	(135-175)mg/m^2 iv	d1	
q3w			

Moore KN, Herzog TJ, Lewin S, et al. A comparison of cisplatin/paclitaxel and carboplatin/paclitaxel in stage IVB, recurrent or persistent cervical cancer. Gynecol Oncol 2007;105:299-303.

Cisplatin +vincristine

Cisplatin	40-50mg/m^2 iv	d1

vincristine	1mg/m^2	iv	d1
10days x 3 course			

Eddy GL, Bundy BN, Creasman WT, et al. Treatment of ("bulky")stage IB cervical cancer with or without neoadjuvant vincristine and cisplatin prior to radical hysterectomy and pelvic/para-aortic lymphadenectomy: a phase III trial of the gynecologic oncology group.Gynecol Oncol 2007;106:362-369. Available at:http://www.ncbi.nlm.nih.gov/pubmed/17493669.

Carboplatin+ vincristine

Carboplatin	AUC (4-6)	iv	d1
vincristine	1mg/m^2	iv	d1
10days x 3 course			

Eddy GL, Bundy BN, Creasman WT, et al. Treatment of ("bulky") stage IB cervical cancer with or without neoadjuvant vincristine and cisplatin prior to radical hysterectomy and pelvic/para-aortic lymphadenectomy: a phase III trial of the gynecologic oncology group.Gynecol Oncol 2007;106:362-369. Available at:http://www.ncbi.nlm.nih.gov/pubmed/17493669.

Cisplatin+Ifosfamide

Cisplatin	(75-100)mg/m^2	iv	d1
Ifosfamide	(3-5)g/m^2	iv	d1
q3w x 6 cycles			

Coleman RE, Harper PG, Gallagher C, et al. A phase II study of ifosfamide in advanced and relapsed carcinoma of the cervix. Cancer Chemother Pharmacol 1986;18:280-283. Available at:http://www.ncbi.nlm.nih.gov/pubmed/3802384.

Carboplatin+Ifosfamide

Carboplatin	AUC (4-6)	iv	d1
Ifosfamide	(3-5)g/m^2	iv	d1
q3w x 6 cycles			

Sutton GP, Blessing JA, McGuire WP, et al. Phase II trial of ifosfamide and mesna in patients with advanced or recurrent squamouscarcinoma of the cervix who had never received chemotherapy: a Gynecologic Oncology Group study. Am J Obstet Gynecol 1993;168:805-807. Available at:http://www.ncbi.nlm.nih.gov/pubmed/8456884.

Cisplatin+ Topotecan

Cisplatin	(75-100)mg/m^2	iv	d1
Topotecan	(2.5-4)mg/m^2	iv	d1
q3w			

1.Long HJ, 3rd, Bundy BN, Grendys EC, Jr., et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a

Gynecologic Oncology Group Study. J Clin Oncol 2005;23:4626-4633.
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3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Carboplatin+ Topotecan

Carboplatin	AUC (4-6)	iv	d1
Topotecan	(2.5-4)mg/m^2	iv	d1
q3w			

1.M A Bookman, H Malmström, G Bolis, et al. Topotecan for the treatment of advanced epithelial ovarian cancer: an open-label phase II study in patients treated after prior chemotherapy that contained cisplatin or carboplatin and paclitaxel.*JCO* October 1998 vol. 16 no. 10 3345-3352
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3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Bevacizumab (Avastin) (自費) **+/- Chemotherapy**

Bevacizumab	7.5 -15mg/kg	iv	d1
Repeat cycle every 3 weeks.			

1.NCCN Clinical Practice Guidelines in Oncology™. Cervical Cancer.v 1.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed February 13, 2012.
2.Monk BJ, Sill MW, Burger RA, Gray HJ, Buekers TE, Roman LD.Phase II trial of bevacizumab in the treatment of persistent or recurrent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2009;27:1069–1074.

Topotecan+/paclitaxel

Topotecan	(2.5-4)mg/m^2	iv	d1
Taxol	(135-175)mg/m^2	iv	d1
q3w			

1.Long HJ, 3rd, Bundy BN, Grendys EC, Jr., et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol 2005;23:4626-4633.
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

CCRT

Cisplatin

Cisplatin	30-50mg/m^2	iv	d1

wk x 6wks

Moore DH, Blessing JA, McQuellon RP, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2004;22:3113-3119.

Carboplatin

Carboplatin	AUC (4-6)	iv	d1
wk x 6wks			

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.

Paclitaxel

Paclitaxel	80mg/m^2	iv	d1
wk x 6 cycles			

Kudelka AP, Winn R, Edwards CL, et al. An update of a phase II study of paclitaxel in advanced or recurrent squamous cell cancer of the cervix. Anticancer Drugs 1997;8:657-661.

Second-Line Therapy

Bevacizumab (Avastin) (自費) **+/- Chemotherapy**

Bevacizumab	7.5-15mg/kg	iv	d1
Repeat cycle every 3 weeks.			

1.NCCN Clinical Practice Guidelines in Oncology™. Cervical Cancer.v 1.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed February 13, 2012.
2.Monk BJ, Sill MW, Burger RA, Gray HJ, Buekers TE, Roman LD.Phase II trial of bevacizumab in the treatment of persistent or recurrent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2009;27:1069–1074.

Docetaxel (Taxotere) (自費)

Docetaxel	100mg/m2 , iv administered over 1 hr.		d1
Repeat cycle every 3 weeks.			

1.NCCN Clinical Practice Guidelines in Oncology™. Cervical Cancer.v 1.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed February 13, 2012.
2.Garcia AA, Blessing JA, Vaccarello L, Roman LD; Gynecologic Oncology Group Study. Phase II clinical trial of docetaxel in refractory squamous cell carcinoma of the cervix: a Gynecologic Oncology Group Study. Am J Clin Oncol. 2007;30:428–431.

Gemcitabine (Gemzar) (自費)

Gemcitabine	800mg/m2 , iv administered over 30 min.	d1
Repeat cycle every 4 weeks.		

1.NCCN Clinical Practice Guidelines in Oncology™. Cervical Cancer.v 1.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed February 13, 2012.
2.Schilder RJ, Blessing J, Cohn DE. Evaluation of gemcitabine in previously treated patients with non-squamous cell carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. Gynecol Oncol. 2005;96:103–107.

Palliative Therapy

Bevacizumab (Avastin) (自費)+/- Chemotherapy

Bevacizumab	7.5-15mg/kg	iv	d1
Repeat cycle every 3 weeks.			

1.NCCN Clinical Practice Guidelines in Oncology™. Cervical Cancer.v 1.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed February 13, 2012.
2.Monk BJ, Sill MW, Burger RA, Gray HJ, Buekers TE, Roman LD.Phase II trial of bevacizumab in the treatment of persistent or recurrent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol. 2009;27:1069–1074.

Cisplatin+Topotecan

Cisplatin	50-100 mg/m^2	iv	d1
Topotecan	0.75mg/m^2		d1-d3
q3w			

1.Long HJ, 3rd, Bundy BN, Grendys EC, Jr., et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol 2005;23:4626-4633.
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3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Cisplatin+ Topotecan

Cisplatin	50-100 mg/m^2	iv	
d1			
Topotecan	(2.5-4)mg/m^2	iv	d1
q3w			

1. HJ, 3rd, Bundy BN, Grendys EC, Jr., et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol 2005;23:4626-4633.
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3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Carboplatin+Topotecan

Carboplatin	AUC (4-6)	iv	d1
Topotecan	0.75mg/m^2		
d1-d3			
q3w			

1.Long HJ, 3rd, Bundy BN, Grendys EC, Jr., et al. Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol 2005;23:4626-4633.
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Carboplatin+ Topotecan

Carboplatin	AUC (4-6)	iv	d1
Topotecan	(2.5-4)mg/m^2	iv	d1
q3w			

1.N. R. Abu-Rustum, S. Lee, L. S. Massad. Topotecan for recurrent cervical cancer after platinum-based therapy.International Journal of Gynecological Cancer, Volume 10, Issue 4, pages 285–288, July/August 2000
2. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings. NIOSH Alert 2004-165.
3. American Society of Health-System Pharmacists. ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-1193.

Cisplatin +paclitaxel+Bevacizumab

paclitaxel	135-175mg/m2	iv	d1
Cisplatin	50-75mg/m2	iv	d1
Bevacizumab	7.5-15mg/kg	iv	d1
21 days intervals			

Tewari KS, Sill MW, Long HJ 3rd,et al. Improved survival with bevacizumab in advanced cervical cancer. N Engl J Med. 2014 Fed 20;370(8):734-43.

Topotecan+paclitaxel+Bevacizumab

paclitaxel	135-175mg/m2	iv	d1
Topotecan	0.75mg/m2	iv	d1- d3
Bevacizumab	7.5-15mg/kg	iv	d1
21 days intervals			

Tewari KS, Sill MW, Long HJ 3rd,et al. Improved survival with bevacizumab in advanced cervical cancer. N Engl J Med. 2014 Fed 20;370(8):734-43

Doxorubicin liposome

Doxorubicin liposome	(25-45)mg/ m^2	iv	d1

q3w

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

Taxol+Lipo-dox

paclitaxel	135-175mg/m2	iv	d1
Doxorubicin liposome d1	(25-45)mg/ m^2	iv	
q3w			

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

Cisplatin+Lipo-dox

Cisplatin d1	75-100 mg/m^2	iv	
Doxorubicin liposome d1	(25-45)mg/ m^2	iv	
q3w			

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

Carboplatin+Lipo-dox

Carboplatin	AUC (4-6)	iv	d1
Doxorubicin liposome d1	(25-45)mg/ m^2	iv	
q3w			

Pujade-Lauraine E, Wagner U, Aavall-Lundqvist E, et al. Pegylated liposomal doxorubicin and carboplatin compared with paclitaxel and carboplatin for patients with platinum-sensitive ovarian cancer in late relapse. J Clin Oncol 2010;28:3323-3329.

Pembrolizumab

Pembrolizumab	100-200 mg	d1
Cycled every 21 days		

Hyun Cheol Chung, MD, PhD, et al.Efficacy and Safety of Pembrolizumab in Previously Treated Advanced Cervical Cancer: Results From the Phase II KEYNOTE-158 Study. Journal of Clinical Oncology 37, no. 17 (June 10, 2019) 1470-1478.

十六、緩和照護原則

若預期疾病難以治癒(如子宮頸癌第四期或是子宮頸癌復發的病人)，病人存活期大於 6 個月，緩和醫療的及早介入能減輕癌症病人及家屬在生理、社會、心理等問題，改善病人生活品質。許多民眾都會將緩和醫療與安寧緩和照護畫上等號，其實它們還是有差異性，當癌病人接受緩和醫療服務時，也可同時併行癌症治療，但接受安寧緩和醫療後，會由安寧緩和醫療團隊接受後續照護，不再有癌症治療介入。(Thomas J et al.2012)

十七、安寧照護原則

若預期疾病難以治癒時，病人存活期小於 6 個月便適合安寧療護(Pomeranz & Brustman, 2005；Waldrop & Rinfrette, 2009) 。若藉由症狀、檢驗數據、及確切的腫瘤診斷，證實臨床上該惡性腫瘤已經廣泛侵犯、或進展快速；功能分數（Palliative Performance Scale）低於 70%；拒絕進一步腫瘤治癒性治療，或者在治療之下仍持續惡化者，即可轉介安寧醫療團隊（彭等，2006）。

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十九、子宮頸癌各期治療完治定義

期別	治療方式	完治定義	備註
0 期	LEEP+ECC	1. 完成 LEEP+ECC or 2. 完成大於 LEEP+ECC 的術式(ATH/LAVH/Extended hysterectomy)	
第 I 期	1.OP 2.RT	1.完成根治性子宮頸切除(Radical Trachelectomy)+骨盆腔淋巴擴清(IA1 可視情形執行淋巴腺擴清)or 2.完成根治性子宮全切除 Radica hysterectomy+骨盆腔淋巴擴清(IA1 可視情形執行淋巴腺擴清)or 3.完成 Pelvic EBRT+Brachytherapy±合併使用鉑金類化學治療	
第 IIA 期	1. OP 2. CCRT 或 3. RT ± C/T	1.完成根治性子宮全切除 Radica hysterectomy+骨盆腔淋巴結±主動脈淋巴結取樣 or 2.完成骨盆腔放射線治療+同步使用含鉑金類化學治療+陰道內放射線治療 or 3.完成骨盆腔放射線治療+使用鉑金類化學治療+陰道內放射線治療	
第 IIB 期	CCRT	完成 CCRT	
第 III 期	CCRT	完成 CCRT	
第 IV 期	1. CCRT or RT 2. Systemic therapy 3. Support care	1.完成 CCRT or RT 療程 2.完成化療≧2 次 3.完成接受標靶治療 2.接受緩和或安寧照護	

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