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
第 2 頁	前言： 我國 2007 年共有 5,252 例子宮頸癌新病例，包括侵襲癌症 1,749 例及原位癌 3,503 例。其粗發生率為每年十萬名婦女 15.41 人；因子宮頸癌死亡人數 833 人，死亡率每十萬人 7.34 人，為女性癌症死亡的第六名。根據 2010 年衛生署公佈 2007 年的癌症統計資料，子宮頸癌排名女性第六大癌症死因，在肺癌、肝癌、結腸直腸癌、胃癌以及乳癌之後，子宮頸癌死亡年齡中位數為 67 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。	前言：修訂為- 我國 2013 年共有 4,683 例子宮頸癌新病例，包括侵襲癌症 1,579 例及原位癌 3,104 例。其粗發生率為每年十萬名婦女 40.06 人；因子宮頸癌死亡人數 702 人，死亡率每十萬人 6.01 人，為女性癌症死亡的第七名。根據 2016 年衛生署公佈 2013 年的癌症統計資料，子宮頸癌排名女性第七大癌症死因，在肺癌、肝癌、結腸直腸癌、胃癌以及乳癌之後，子宮頸癌死亡年齡中位數為 67 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。
	前言： Practice Guide-lines in Cervical Cancer 2010 版	前言：修訂為- Practice Guide-lines in Cervical Cancer 2017 版
第 16 頁	單純式子宮切除後意外發現子宮頸侵襲癌： 組織病理分期 IA1→切除邊緣侵襲或影像檢查轉移 →子宮頸旁組織全切除及部分陰道切除及骨盆淋巴結摘除或併主動脈旁淋巴結摘除或觀察追蹤 →影像檢查淋巴結轉移→考慮對明顯變大之淋巴結進行癌減積手術→1.骨盆放射治療及陰道近接治療或併鉑類化合物化療 2.子宮頸旁組織全切除及部分陰道切除及骨盆淋巴結摘除或併主動脈旁淋巴結摘除	單純式子宮切除後意外發現子宮頸侵襲癌：修訂為- 組織病理分期 IA1→無切除邊緣侵襲；無影像檢查轉移無淋巴血管間隙侵襲→觀察追蹤
	單純式子宮切除後意外發現子宮頸侵襲癌： 組織病理分期≧IA2 →無切除邊緣侵襲無影像檢查轉移→1.骨盆放射治療及陰道近接治療或併鉑類化合物化療 2.子宮頸旁組織全切除及部分陰道切除及骨盆淋巴結摘除或併主動脈旁淋巴結摘除 →切除邊緣侵襲或影像檢查轉移 →影像檢查無淋巴結轉移→1.骨盆放射治療及陰道近接治 療或併鉑類化合物化療 2.子宮頸旁組織全切除及部分陰道切除及骨盆淋巴結摘除或併主動脈旁淋巴結摘除 →影像檢查淋巴結轉移→考慮對明顯變大之淋巴結進行癌減積手術→1.骨盆放射治療及陰道近接治療或併鉑類化合物化療 2.子宮頸旁組織全切除及部分陰道切除及骨盆淋巴結摘除或併主動脈旁淋巴結摘除	單純式子宮切除後意外發現子宮頸侵襲癌：修訂為- (第 16 頁及第 17 頁合併) 組織病理分期≧IA1 併淋巴血管間隙侵襲→ →無切除邊緣侵襲無影像檢查轉移 →骨盆放射治療＋陰道近接治療±鉑類化合物化療→觀察追蹤 →子宮頸旁組織全切除＋上陰道切除＋骨盆淋巴結摘除±主動脈旁淋巴結摘除 →無淋巴結轉移→觀察追蹤 →骨盆放射治療±陰道近接治療(若有間質浸潤或淋巴血管間隙侵襲) →淋巴結轉移或切除邊緣侵襲或子宮頸旁組織侵襲→骨盆放射治療(若有主動脈旁淋巴結侵襲)＋鉑類化合物化療±陰道近接治療(若

第 17 頁	單純式子宮切除後意外發現子宮頸侵襲癌： A. 子宮頸旁組織全切除及部分陰道切除(complete parametrectomy)及骨盆淋巴結摘除或併主動脈旁淋巴結摘除 →無淋巴結轉移無陰道切除邊緣侵襲無子宮旁組織侵襲→觀察，或若腫瘤較大、子宮頸基質組織深部或有淋巴血管內侵襲，可觀察或安排骨盆放射治療，＋/－併陰道近接治療 →淋巴結轉移，或陰道切除邊緣侵襲，或子宮旁組織侵襲→骨盆或併主動脈旁放射治療及同時合併 cisplatin 化療＋/－ 陰道近接治療(如有陰道切除邊緣侵襲，必須給予陰道近接治療) B. 骨盆放射治療及陰道近接治療或併鉑類化合物化療	有陰道邊緣侵襲) →切除邊緣侵襲或影像檢查轉移 →影像檢查無淋巴結轉移→骨盆放射治療(若有主動脈旁淋巴結侵襲)＋鉑類化合物化療±陰道近接治療(若有陰道邊緣侵襲) →影像檢查淋巴結轉移→考慮對明顯變大之淋巴結進行癌減積手術→骨盆放射治療(若有主動脈旁淋巴結侵襲)＋鉑類化合物化療±陰道近接治療(若有陰道邊緣侵襲)
第 24 頁	化學治療： First-line combination therapy Second-line therapy	化學治療：修訂為- First-line combination therapy： 新增 Carboplatin/paclitaxel/bevacizumab 新增 Topotecan/paclitaxel Second-line therapy： 新增 Albumin-bound paclitaxel

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2013年共有 4,683例子宮頸癌新病例，包括侵襲癌症 1,579例及原位癌 3,104例。其粗發生率為每年十萬名婦女 40.06人；因子宮頸癌死亡人數 702人，死亡率每十萬人 6.01人，為女性癌症死亡的第七名。根據 2016年衛生署公佈 2013年的癌症統計資料，子宮頸癌排名女性第七大癌症死因，在肺癌、肝癌、結腸直腸癌、胃癌以及乳癌之後，子宮頸癌死亡年齡中位數為 67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 Cancer 2017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。影像檢查，包括超音波、電腦斷層攝影或核磁共振檢查等，不應使用於尚未經病理組織確認為侵襲性子宮頸癌的患者。

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

子宮頸癌的分期主要以臨床評估為主，國際婦產科聯盟 (International Federation of Gynecology and Obstetrics, FIGO) 1994 年的分期，僅使用胸部 X 光(chest X-ray)、腎盂攝影及鋇劑浣腸攝影 (barium enema) 等影像檢查做為分期的參考。FIGO 一向堅持分期只是為了比較的目的，而不是為了治療的指引。

淋巴攝影 (lymphangiography)、核磁共振或電腦斷層檢查，對於治療的規劃可能有所幫助，但檢查的結果並不影響既有的分期。

FIGO分期的侵襲性檢查則限制在陰道鏡、子宮頸切片、子宮頸錐狀手術、膀胱鏡及直腸鏡等。腹腔鏡、子宮鏡、及後腹腔探查手術並不做為分期診斷的依據。

國際婦產科聯盟 (International Federation of Gynecology and Obstetrics, FIGO)於 2009 年提出子宮頸侵襲癌分期修定，主要將分期 IIA 細分為 IIA1 及 IIA2。 兩者之間以腫瘤大小 4 公分為分界，腫瘤最大徑小於等於 4 公分者為 IIA1，腫瘤最大徑大於 4 公分者為 IIA2。修正後分期如下表所列：

FIGO 分期		TNM Categories
	Primary tumor cannot be assessed. (主要腫瘤無法評估)	**Tx**
	No evidence of primary tumor. (沒有腫瘤之證據)	**T0**
0	Carcinoma in situ (pre-invasive carcinoma). (原位癌)	**Tis**
I	Cervical carcinoma confined to uterus (extension to corpus should be disregarded). (子宮頸癌侷限在子宮)	**T1**
IA	Invasive carcinoma diagnosed only by microscopy. (微侵襲癌)	**T1a**

FIGO 分期		TNM Categories
IA1	Stromal invasion no greater than 3.0 mm in depth and 7.0 mm or less in horizontal spread. (微侵襲癌，水平徑不超過 7 毫米，子宮頸基質侵襲不超過基底膜下 3 毫米)	**T1a1**
IA2	Stromal invasion more than 3.0 mm and not more than 5.0 mm with a horizontal spread 7.0 mm or less. (微侵襲癌，水平徑不超過 7 毫米，子宮頸基質侵襲為基底膜下 3-5 毫米之間)	**T1a2**
IB	Clinically visible lesion confined to the cervix or microscopic lesion greater than IA2 / T1a2. (肉眼可見腫瘤侷限在子宮頸或顯微病灶範圍超出IA2/ T1a2)	**T1b**
IB1	Clinically visible lesion 4.0 cm or less in greatest dimension. (子宮頸腫瘤直徑不超過 4 公分)	**T1b1**
IB2	Clinically visible lesion more than 4.0 cm in greatest dimension. (子宮頸最大腫瘤直徑超過 4 公分)	**T1b2**
II	Tumor invades beyond the uterus but not to pelvic wall or lower third of vagina. (腫瘤侵襲已達子宮頸外組織，但未達骨盆壁及陰道下端 1/3)	**T2**
IIA	Without parametrial invasion. (無子宮頸旁組織侵襲)	**T2a**
IIA1	**Clinically visible lesion ≤4.0 cm in greatest dimension** (子宮頸腫瘤直徑不超過 4 公分)	**T2a1**
IIA2	**Clinically visible lesion N4 cm in greatest dimension** (子宮頸最大腫瘤直徑超過 4 公分)	**T2a2**
IIB	With parametrial invasion. (已有子宮頸旁組織侵襲)	**T2b**

FIGO 分期		TNM Categories
III	Tumor extends to pelvic wall and/or involves lower third of vagina and/or causes hydronephrosis or non-functional kidney. (腫瘤侵襲達骨盆壁或達陰道下端 1/3 或造成腎臟水腫或無功能腎臟)	**T3**
IIIA	Tumor involves lower third of vagina, no extension to pelvic wall. (腫瘤侵襲達陰道下端 1/3，未達骨盆壁)	**T3a**
IIIB	Tumor extends to pelvic wall and/or causes hydronephrosis or non-functional kidney. (腫瘤侵襲達骨盆壁或造成腎臟水腫或無功能腎臟)	**T3b**
IVA	Tumor invades mucosa of bladder or rectum and/or extends beyond true pelvis. (腫瘤侵襲膀胱或直腸之黏膜層，或延展超過真骨盆腔)	**T4**
IVB	Distant metastasis. (遠處轉移)	**M1**

五、 首次治療

子宮頸癌首次診斷後的治療，必須根據仔細的臨床評估：

分期	治療前檢查	選擇性檢查
＜IB1	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.子宮頸錐狀手術(保持生殖能力者) 5.胸部 X 光 6.常規生化檢驗	1.分期為IB2 或以上者，膀胱或直腸鏡檢 2.血清腫瘤標記檢驗 (SCC、CEA；腺癌者 CEA、CA-125) 3.葡萄糖正子攝影
≧IB1	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.胸部X光 5.安排腎盂攝影(IVP)或腹部及骨盆電腦斷層或核磁共振檢查 6.常規生化檢驗	1.分期為IB2 或以上者，膀胱或直腸鏡檢 2.血清腫瘤標記檢驗 (SCC、CEA；腺癌者 CEA、CA-125) 3.葡萄糖正子攝影

早期的子宮頸癌，以手術治療為主，包括：

1. FIGO 分期 IA1：
   (1) 筋膜外 (extrafascial)子宮切除，若同時有陰道癌前病變，亦需適當的切除。對希望保留生育能力且子宮頸錐狀手術切除標本邊緣為陰性者，可考慮以較密集的追蹤取代子宮切除手術。如果標本邊緣呈現原位癌變化，可以再次施行病變區切除或子宮頸錐狀手術。**(Level of Evidence 2a)**
   (2) 若子宮頸錐狀手術標本發現子宮頸基質之淋巴血管腔已有腫瘤細胞侵入，或可考慮較小範圍(modified)即第二型 (Type 2) 根治性子宮切除和骨盆淋巴結摘除。如果希望保留生育能力，可依據下述 IA2原則處理，惟尚未有明確證據。**(Level of Evidence 2b)**

2. FIGO 分期 IA2：
   (1) 較小範圍 (modified) 即第二型 (Type 2) 根治性子宮切除和骨盆淋巴結摘除或併主動脈旁淋巴結取樣。如果希望保留生育能力，可選擇：
      (A)根治性子宮頸切除 (radical trachelectomy) 及骨盆淋巴結摘除手術或併主動脈旁淋巴結取樣。
      (Level of Evidence 2b)
      (B)子宮頸大範圍錐狀手術及骨盆淋巴結摘除手術，但此仍有爭議。
   (2)對於身體狀況不適合手術者，可以採取近接放射治療併骨盆放射治療。

3. FIGO 分期 IB1 或 IIA1 者：
   (1) 根治性子宮切除及骨盆淋巴結摘除或併主動脈旁淋巴結取樣。
   (2) 對於身體狀況不適合手術者，可以採取骨盆放射治療合併近接放射治療。 **(Level of Evidence 1b)**

4. FIGO 分期 IB2 或 IIA2 者：
   (1) 合併放射線及 cisplatin 化學治療。
   (2) 根治性子宮切除和骨盆淋巴結摘除或併主動脈旁淋巴結取樣。

(3) 術前化學治療後接續根治性子宮切除和骨盆淋巴結摘除或併主動脈旁淋巴結取樣。
(Level of Evidence Ib, Grade of Recommendation A)

(4) 合併放射線及 cisplatin 化學治療(但未完成近接電療者)，接續子宮切除。

5. FIGO 分期 IIB － IVA 者：

(1)骨盆淋巴結轉移無主動脈旁淋巴結轉移者，同時合併化療及骨盆或併主動脈旁淋巴結放射治療及近接治療。

(2)骨盆淋巴結轉移主動脈旁淋巴結轉移者，同時合併化療及骨盆併主動脈旁淋巴結放射治療及近接治療。**(Level of Evidence 2A, Grade of Recommendation B)**

6. FIGO 分期 IVB 者：可行時施行切片確認，給予全身性化學治療或併選擇性放射治療。
(Level of Evidence 2A, Grade of Recommendation B)

7.年輕女性為保留生殖能力，如確診為子宮頸侵襲癌後可以如下處置：

Management	FIGO
Cervical conization	Ia1
Radical trachelectomy with lymphadenectomy	• Ia1 with淋巴血管間隙侵犯LVSI ＊可考慮子宮頸錐狀切除術(conization)+雙側骨盆腔淋巴結摘除BPLND(Bilateral pelvic lymph nodes dissectiotn) • Ia2 ＊可考慮conization+BPLND • Ia adenocarcinoma • Ib <2 cm with limited endocervical involvement and lymph node metastases

New Classification

- **Type A Hysterectomy**
  - Minimum resection of paracervix

- **Type B Hysterectomy(Modified Radical Hysterectomy)**
  - B1:Transection of paracervix at the ureter
  - B2:Additional removal of lateral paracervical lymph node（medial to Obturator nerve）

- **Type C Hysterectomy(Radical Hysterectomy)**
  - Transetion of paracervix at the junction with internal iliac vascular systern
  - C1:Nerve preservation of autonomic nerves
  - C2:Without preservation of autonomic nerves

- **Type D Hysterectomy**
  - Laterally extended resection
  - D1:Resection of total paracervix at pelvic side wall and vessels of paracervix
  - D2:D1+hypogastric vessel and adjacent fascial or muscular structure

- **Lymph node dissection**
  - Level1:Inter and exernal iliac lymph node
  - Level2:Common iliac lymph node
  - Level3:Inframesenteric aortic
  - Level4:Infrarenal aortic

子宮頸侵襲癌治療指引

FIGO 分期 IA1

1.筋膜外子宮切除術
2.欲保留生育能力者，於子宮頸錐狀手術(Trachelectomy)後密集追蹤觀察
3.若子宮頸錐狀手術標本發現子宮頸基質之淋巴血管腔已有腫瘤細胞侵入，較小範圍根治性子宮切除術及骨盆淋巴結摘除術，或合併主動脈旁淋巴結取樣。或可骨盆腔放射治療加陰道近接放射治療。
4.若子宮頸錐狀手術標本發現切除邊緣受侵襲(positive margins for dysplasia or carcinoma)，應作筋膜外或 modified 子宮切除術，若切除邊緣受侵襲為 carcinoma 者，則加作 BPLND。或考慮重新作子宮頸錐狀手術評估侵犯深度。

FIGO 分期 IA2

1.較小範圍根治性子宮切除術及骨盆淋巴結摘除術，或併主動脈旁淋巴結取樣或
2.近接治療併骨盆放射治療＊或
3.欲保留生育能力者，可施行根治性子宮頸切除術及淋巴結摘除術或conization+BPLND

FIGO 分期 IB1 或 IIA1

1.根治性子宮切除術及骨盆淋巴結摘除術，或合併主動脈旁淋巴結取樣或
2.CCRT＊或
3.欲保留生育能力者，可執行根治性子宮頸切除術及淋巴結摘除術**(Tumor size<3cm)**

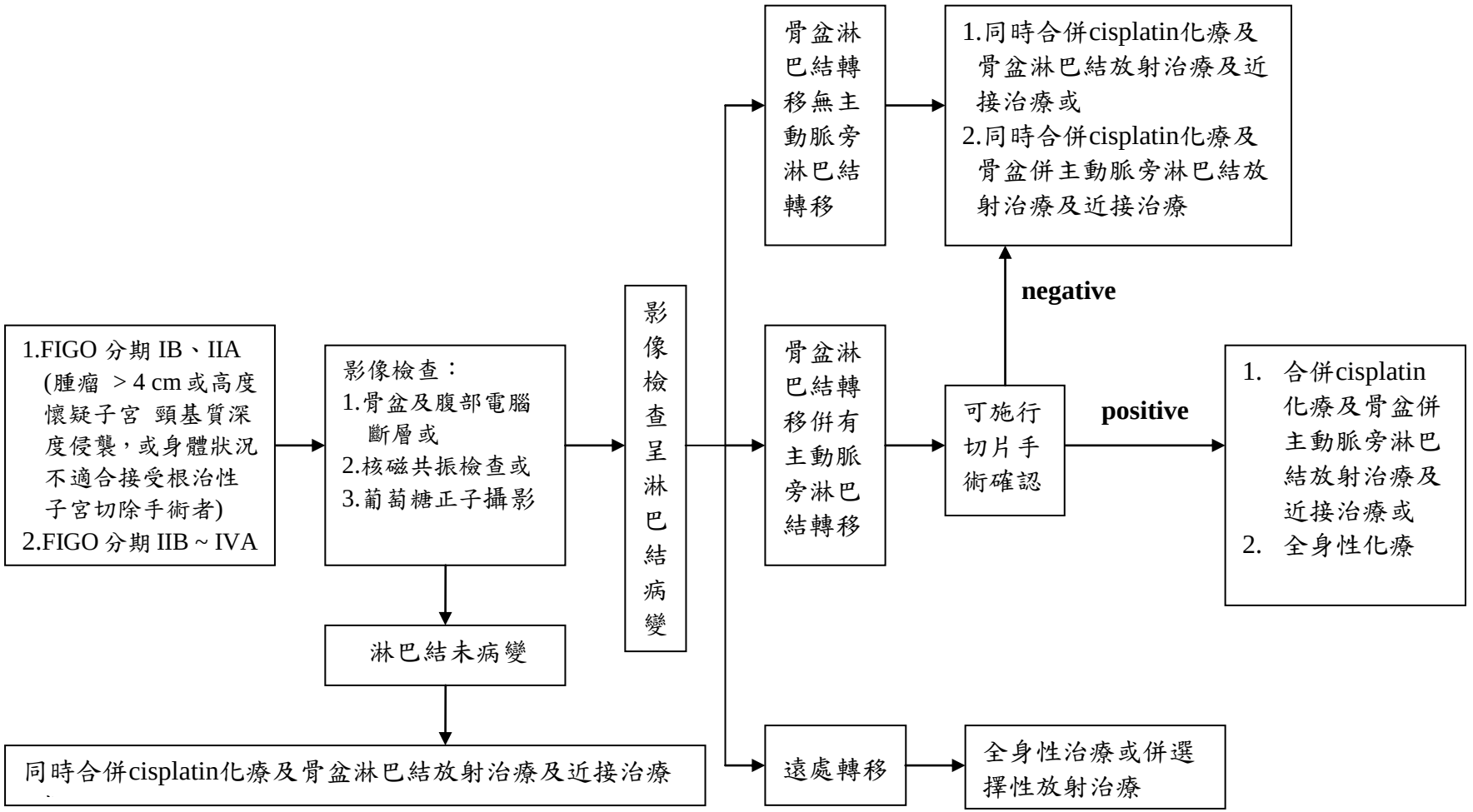
FIGO 分期 IB2 或 IIA2

1.CCRT＊或
2.根治性子宮切除術及骨盆淋巴結摘除術，建議合併主動脈淋巴節取樣或
3.三回合術前化學治療後，根治性子宮切除術及骨盆淋巴結摘除術
4.欲保留生育能力者，可給予Neoadjuvant化學治療，再繼續施行根治性子宮頸切除術及淋巴結摘除術 (Tumor size3-4cm)

手術標本組織病理檢查

- 無淋巴結轉移，無陰道切除邊緣侵襲且無子宮旁組織侵襲 → 1.觀察 2.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)可安排骨盆放射治療。
- ＞2/3Cervix 深度及 LVSI (＋) / Full thicknes +Bulky → CCRT/RT(option)
- 淋巴結轉移或陰道切除邊緣侵襲或子宮旁組織侵襲 → 1.淋巴結轉移者，需施行化學放射治療 2.無淋巴結轉移者，CCRT 3.陰道切除邊緣呈現侵襲性病灶，應施行陰道近接放射治療

淋巴血管間隙侵犯 LVSI: Vascular/lymphatic invasion　　子宮頸錐狀切除術(conization)+雙側骨盆腔淋巴結摘除 BPLND(Bilateral pelvic lymph nodes dissectiotn)


1.FIGO 分期 IB、IIA
(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 ~ IVA
影像檢查：
1.骨盆及腹部電腦斷層或
2.核磁共振檢查或
3.葡萄糖正子攝影
影像檢查呈淋巴結病變
淋巴結未病變
同時合併cisplatin化療及骨盆淋巴結放射治療及近接治療
骨盆淋巴結轉移無主動脈旁淋巴結轉移
骨盆淋巴結轉移併有主動脈旁淋巴結轉移
遠處轉移
1.同時合併cisplatin化療及骨盆淋巴結放射治療及近接治療或
2.同時合併cisplatin化療及骨盆併主動脈旁淋巴結放射治療及近接治療
negative
可施行切片手術確認
positive
1. 合併cisplatin化療及骨盆併主動脈旁淋巴結放射治療及近接治療或
2. 全身性化療
全身性治療或併選擇性放射治療

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淋巴結轉移、腫瘤組織侵襲達子宮頸旁組織或手術標本邊緣時，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、腫瘤組織侵襲達子宮頸旁組織或手術標本邊緣等復發高風險因子，2015年NCCN仍建議考慮依據LVSI情形、子宮基質侵犯深度、主要腫瘤大小(依據臨床觸診)等危險因子加作骨盆腔放射治療之輔助性放療。

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

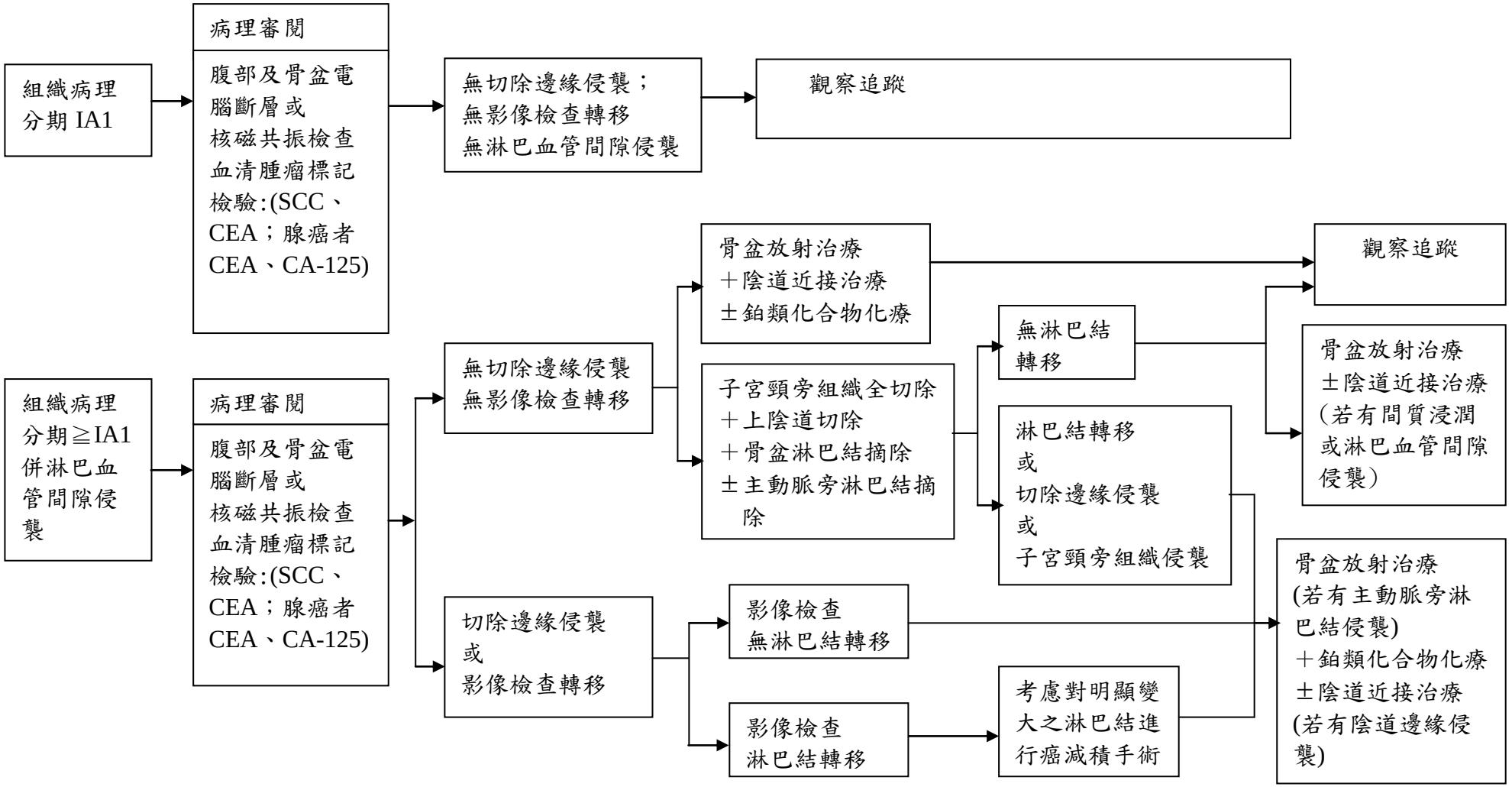
本院臨床指引建議對於具有復發高風險因子個案應給予術後輔助治療 (Pelvic RT + concurrent cisplatin containing chemotherapy) 。而針對中度風險因子個案，可以再就手術的範圍，決定是否安排術後輔助性放療。

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IA2或更高) 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，建議施行放射治療和陰道近接治療；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cisplatin及放射治療。**(Level of Evidence 3b)**

術後評估的風險因子中，FIGO 分期、淋巴結轉移、子宮頸基質侵襲超過1/3、中度或不良的分化、陽性的HPV 18對於之後的復發具有顯著的影響；而FIGO分期、淋巴結轉移、子宮頸基質侵襲超過1/3、子宮頸旁組織的侵襲、陽性的HPV 18 及年紀大於等於45歲則是死亡的預測因子。
(from Journal of clinical oncology 25(24) 2007, 3628-34. level of evidence 3a, Grade of recommendation B)

單純式子宮切除後意外發現有子宮頸侵襲癌臨床指引



八、 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個月一次抹片檢查，第三年每4個月一次，第四至五年則每6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) 及血清腎功能標記 (BUN, creatinine) 檢驗。

4. 每年可給予胸部 X 光檢查。

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。

九、 復發或持續性疾病的治療 (Salvage Therapy)

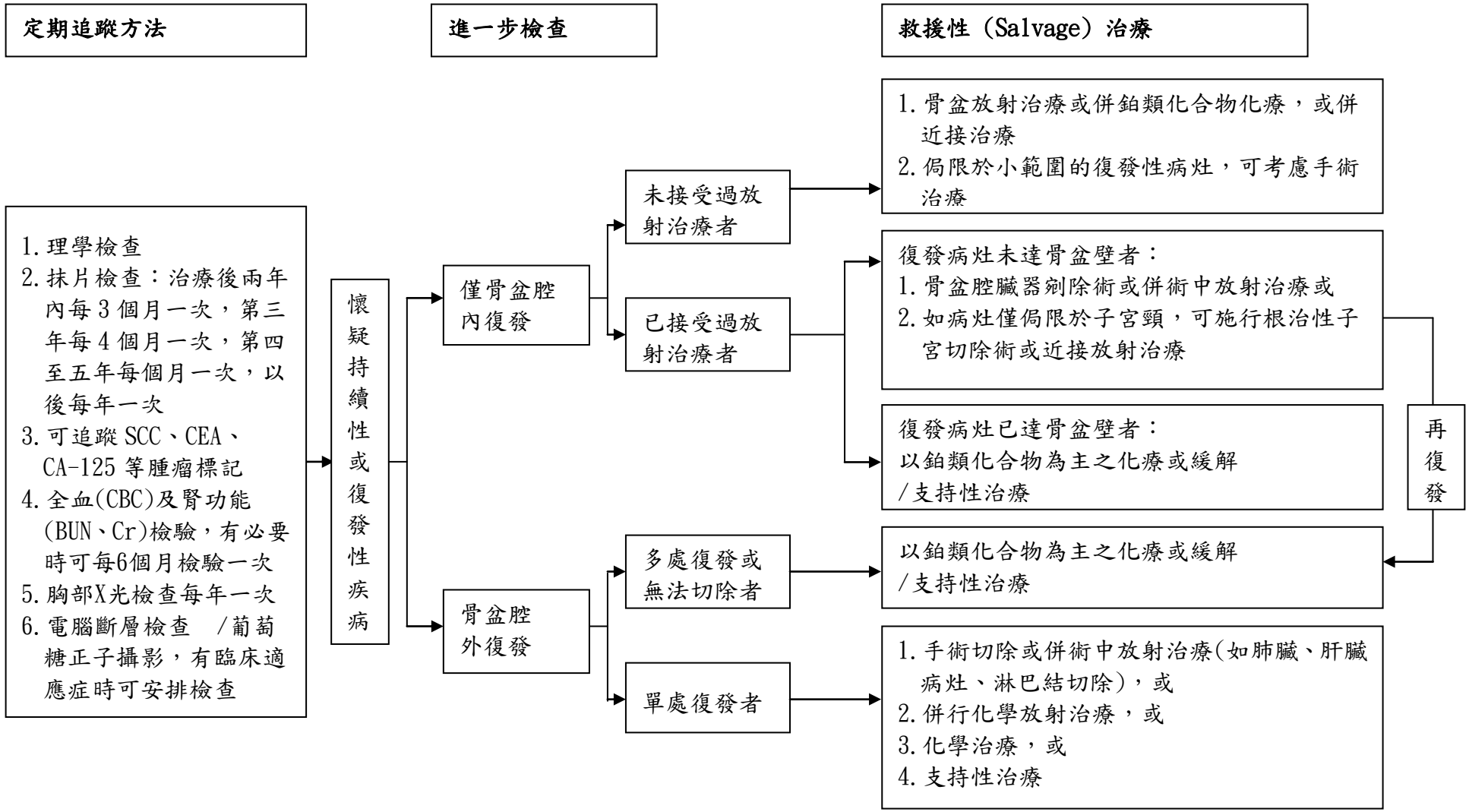
子宮頸癌完全治療後，一但發現有復發情形，除非只是陰道的上皮內病變，否則皆應先安排充分的檢查，包括詳細的理學及影像學檢查，如全身電腦斷層檢查或胸部 X光及腹部及骨盆電腦斷層檢查或核磁共振檢查、腫瘤標記檢驗等，以了解全般情況。如果可能，也應選取代表性的可疑病灶，進行切片或細針抽吸取樣，以確定復發。如果懷疑復發的部位僅侷限於單側肺部，而並無主動脈旁淋巴結腫大的情形，必須盡可能排除原發性肺癌的可能性。

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 和 topotecan ；而可能使用的第一線合併化學藥物治療有 cisplatin / paclitaxel、 cisplatin / topotecan、 cisplatin / ifosfamide 及 carboplatin / paclitaxel。 Cisplatin被認為是緩和治療最有效的藥物，其腫瘤反應率約 20% 到 30%。偶而可以見到腫瘤完全消失的情形。 Carboplatin也有 19% 的反應率；其它可以使用的藥物包括 ifosfamide、 epirubicin 和vinorelbine，反應期間通常是 3 至 6 個月，平均存活約 1 年。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



十、 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。

(Level of Evidence 2A, Grade of Recommendation B)
(Radiother Oncol. 1992 Dec;25(4):273-9.)
(Int J Radiat Oncol Biol Phys. 1993 Feb 15;25(3):391-7.)

十一、 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 : 4.5-5.5 Gy x 4-6 Fractions	Point A: 75~80Gy
IB1& IIA1 (tumor < 4cm)	External beam : Pelvic irradiation to 45~55Gy ICBT : 4.5-5.5 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

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 Gy IVBT : 4.5-5 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 : 4.5-5 Gy x 3-4 Fractions

IVBT: intravaginal brachytherapy

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

十二、化學治療

分類：

First-line combination therapy	Possible first-line single agent therapy	Second-line therapy (All agents listed are category 2B)
★Cisplatin / paclitaxel(category 1) ★Cisplatin/paclitaxel/Bevacizumab (category 1) ★Topotecan/paclitaxel/Bevacizumab (category 1) ★Carboplatin / paclitaxel ★Carboplatin/paclitaxel/bevacizumab ★Cisplatin / topotecan ★Topotecan/paclitaxel ★Cisplatin / gemcitabine(category 2B)	★Cisplatin(preferred as a single agent) ★Carboplatin ★Paclitaxel	★Bevacizumab ★Albumin-bound paclitaxel ★Docetaxel ★Epirubicin ★5-FU(5-fluorouracil) ★Gemcitabine ★Ifosfamide ★Vinorelbine ★Irinotecan ★Liposomal ★Doxorubicin ★Mitomycin ★Pemetrexed ★Topotecan ★Vinorelbine

Neoadjuvant

Cisplatin

Cisplatin	(50/75/100)mg/m^2	iv	d1
10days x3 course			

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
10days x 3 course			

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.

Carboplatin+Paclitaxel

Carboplatin	AUC (4-6)	iv	d1
Paclitaxel	80mg/m^2	iv	d1
10days x 3 course			

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+Paclitaxel

Cisplatin	(40/50)mg/m2	iv	d1
Paclitaxel	80mg/m^2	iv	d1
10days x 3 course			

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.

Cisplatin +Oncovin

Cisplatin	(40/50)mg/m^2	iv	d1
Oncovin	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 + Topotecan

Cisplatin	(40/50)mg/m^2	iv	d1
Topotecan	(2.5-4)mg/m^2	iv	d1
10days x 3 course			

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+ Oncovin

Carboplatin	AUC (4-6)	iv	d1
Oncovin	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+ Topotecan

Carboplatin	AUC (4-6)	iv	d1
Topotecan	(2.5-4)mg/m^2	iv	d1
10days x 3 course			

1.N. Manci, C. Marchetti, C. Di Tucci, et al. A prospective phase II study of topotecan (Hycamtin®) and cisplatin as neoadjuvant chemotherapy in locally advanced cervical cancer.Gynecologic Oncology, Volume 122, Issue 2, August 2011, Pages 285–290
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.

Adjuvant chemotherapy

Cisplatin

Cisplatin	(40/50)mg/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.

Paclitaxel(自費)

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.

Cisplatin+Etoposide

Cisplatin	(40/50)mg/m^2	iv	d1
Etoposide	(75-100)mg/m^2	iv	d1
wk x 6 cycles			

Jeong-Hoon Baea, Sung-Jong Leea, Ahwon Leeb,et al. Neoadjuvant cisplatin and etoposide followed by radical hysterectomy for stage 1B – 2B cervical cancer. Gynecologic Oncology Volume 111, Issue 3, December 2008, Pages 444 – 448

Cisplatin+Etoposide

Cisplatin	(75-100)mg/m^2	iv	d1
Etoposide	(75-100)mg/m^2	iv	d1
q3w x 6 cycles			

Jeong-Hoon Baea, Sung-Jong Leea, Ahwon Leeb,et al. Neoadjuvant cisplatin and etoposide followed by radical hysterectomy for stage 1B – 2B cervical cancer. Gynecologic Oncology Volume 111, Issue 3, December 2008, Pages 444 – 448

Carboplatin+Etoposide

Carboplatin	AUC (4-6)	iv	d1
Etoposide	(75-100)mg/m^2	iv	d1
wk x 6 cycles			

Mitchell Morris, M.D., David M. Gershenson, M.D., Patricia Eifel, M.D., et al. Treatment of small cell carcinoma of the cervix with cisplatin, doxorubicin, and etoposide.Gynecologic Oncology, Volume 47, Issue 1, October 1992, Pages 62–65

Carboplatin+Etoposide

Carboplatin	AUC (4-6)	iv	d1
Etoposide	(75-100)mg/m^2	iv	d1
q3w x 6 cycles			

Mitchell Morris, M.D., David M. Gershenson, M.D., Patricia Eifel, M.D.,et al. Treatment of small cell carcinoma of the cervix with cisplatin, doxorubicin, and etoposide.Gynecologic Oncology, Volume 47, Issue 1, October 1992, Pages 62–65

Carboplatin+Paclitaxel (自費)

Carboplatin	AUC (4-6)	iv	d1
Paclitaxel	80mg/m^2	iv	d1
q3wk x 6 cycles			

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+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 +Paclitaxel(自費)

Cisplatin	(75-100)mg/m^2	iv	d1
Paclitaxel	80mg/m^2	iv	d1
q3wk x 6 cycles			

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.

Cisplatin+ Topotecan

Cisplatin	(75-100)mg/m^2	iv	d1
Topotecan	(2.5-4)mg/m^2	iv	d1
10days x 3 course			

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
10days x 3 course			

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
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	(30/40/50)mg/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.

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.

Cisplatin + 5-FU

Days 1 and 29: 4 hrs prior to external-beam radiotherapy: Cisplatin 50mg/m^2 iv infusion at 1mg/min with standard hydration, plus Days 2–5, and 30–33: 5-FU 1000mg/m^2 iv continuous infusion over 24 hrs(total dose 4000mg/m^2 each course).

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.Whitney CW, Sause W, Bundy BN, et al. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiotherapy in stage IIB-IVA carcinoma of the cervix
with negative para-aortic lymph nodes: A Gynecologic Oncology Group and Southwest Oncology Group study. J Clin Oncol.1999;17:1339–1348.

Cisplatin + 5-FU

Days 1–5 of radiotherapy: Cisplatin 75mg/m^2 iv over 4 hrs followed by 5-FU 4000mg/m^2 iv over 96 hrs. Repeat cycle every 3 weeks for 2 additional cycles.

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.Morris M, Eifel PF, Lu J, et al. Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. NEJM. 1999;340(15):1137–1143.

Cisplatin + 5-FU +hydroxyurea

Days 1 and 29: Cisplatin 50mg/m^2 iv followed by 4000mg/m^2 5-FU over 96 hrs; hydroxyurea 2g orally twice weekly for 6 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.Rose PG, Bundy BN, Watkins EB, et al. Concurrent cisplatinbased radiotherapy and chemotherapy for locally advanced cervical cancer. NEJM. 1999;340:1144–1153.

Cisplatin + gemcitabine +radiotherapy+ brachytherapy

Induction therapy Days 1, 8, 15, 22, 29 and 36: Cisplatin 40mg/m^2 + gemcitabine 125mg/m^2 + concurrent external-beam radiotherapy 50.4Gy in 28 fractions, followed by brachytherapy 30–35Gy in 96 hrs. Adjuvant therapy Day 1: Cisplatin 50mg/m^2, plus Days 1 and 8: Gemcitabine 1,000mg/m^2. Repeat every 3 weeks for 2 cycles.

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.Duenas-Gonzalez A, Zarba JJ, Patel F, et al. Phase III, open-label,randomized study comparing concurrent gemcitabine plus isplatin and radiation followed by adjuvant emcitabine and isplatin versus concurrent cisplatin and radiation in patients with stage IIB to IVA carcinoma of the cervix. J Clin Oncol.2011;29(13):1678–1685.

Second-Line Therapy

Bevacizumab (Avastin)（自費）

Bevacizumab	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

Cisplatin+Topotecan

Cisplatin	(50/75/100) 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.
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+Taxol

Cisplatin	(50/75/100) mg/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.
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+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+ Topotecan

Cisplatin	(50/75/100)mg/m^2	iv	d1
Topotecan	(2.5-4)mg/m^2	iv	d1
10days x 3 course			

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.
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
10days x 3 course			

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 or 175 mg/m2	iv	d1
Cisplatin	50mg/m2	iv	d1
Bevacizumab	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	175 mg/m2	iv	d1
Topotecan	0.75mg/m2	iv	d1- d3
Bevacizumab	15mg/kg	iv	d1
21 days intervals x			

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

十三、安寧緩和照護原則

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，即可轉介緩和醫療團隊（彭等，2006）。

十四、參考文獻

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5. Cervical Cancer (PDQR): Treatment, Health Professional Version. National Cancer Institute. 2003.
6. Resbeut M, Fondrinier E, Fervers B, et al. Standards, Options and Recommendations for the management of invasive cervical cancer patients (non metastastic). Bulletin du Cancer 2003; 90:333-346.
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