高 雄 榮 民 總 醫 院

皮膚癌(SCC)診療原則

2018年01月23日 第一版

皮膚癌醫療團隊擬定

注意事項：這個診療原則主要作為醫師和其他保健專家診療癌症病人參考之用。假如你是一個癌症病人，直接引用這個診療原則並不恰當，只有你的醫師才能決定給你最恰當的治療。

修訂指引

- 本共識依下列參考資料修改版本
  - NCCN 2016版 診療指引

SCC診療指引審視修訂會議討論日期

- 上次會議：2017/03/21
- 本共識經審視後與上一版之差異

上一版:	新版:
一、使用NCCN 2017版 診療指引 二、修改治療方式	一、更新 NCCN 2018版 診療指引 二、修改治療方式 1.初始治療增加± C/T or Cryotherapy 2.修改Chemotherapy regimen處方用藥 ◆ 增加Metastasis藥物

鱗狀上皮細胞癌(SCC)

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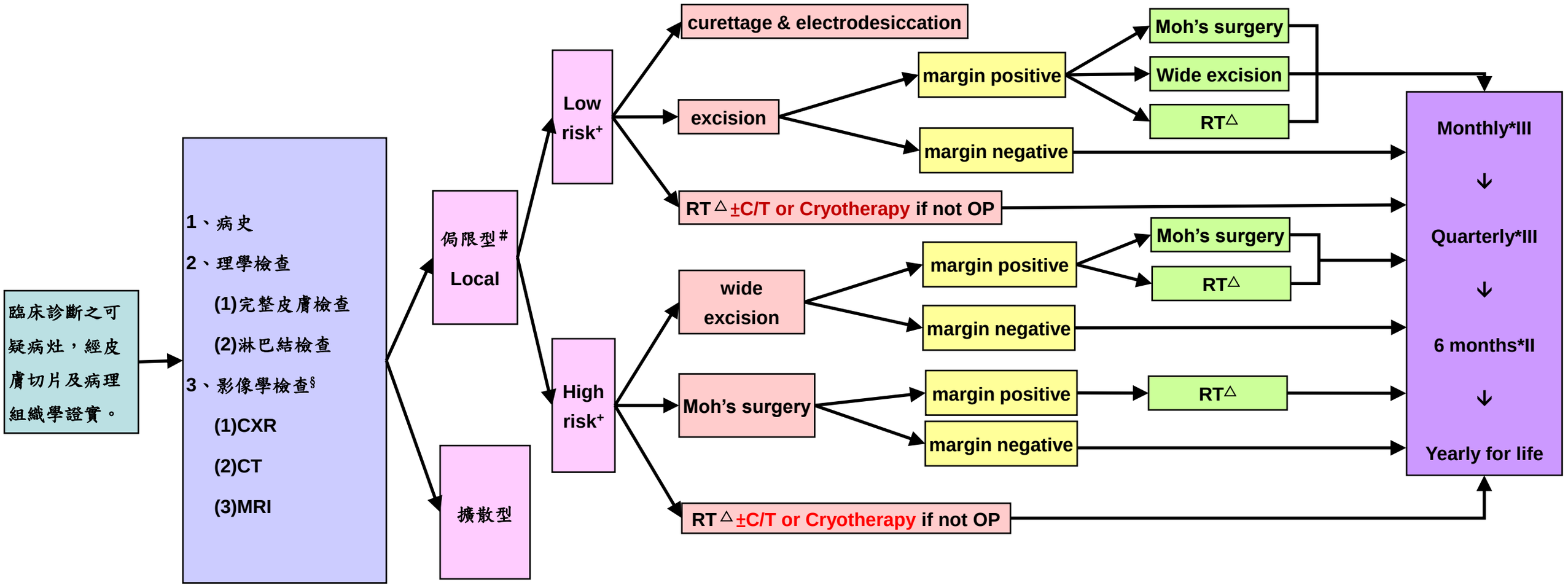
臨床診療指引 2018第一版

診斷	初步評估	分期	初始治療	療效評估	輔助治療	追蹤



§： Image studies is indicated for extensive disease (deep structural involvement such as bone, deep soft tissue, perineural disease)

＋：附件一

△： RT主要針對手術不適用之情形, 附件二

＃： T any, N0, M0, 附件三

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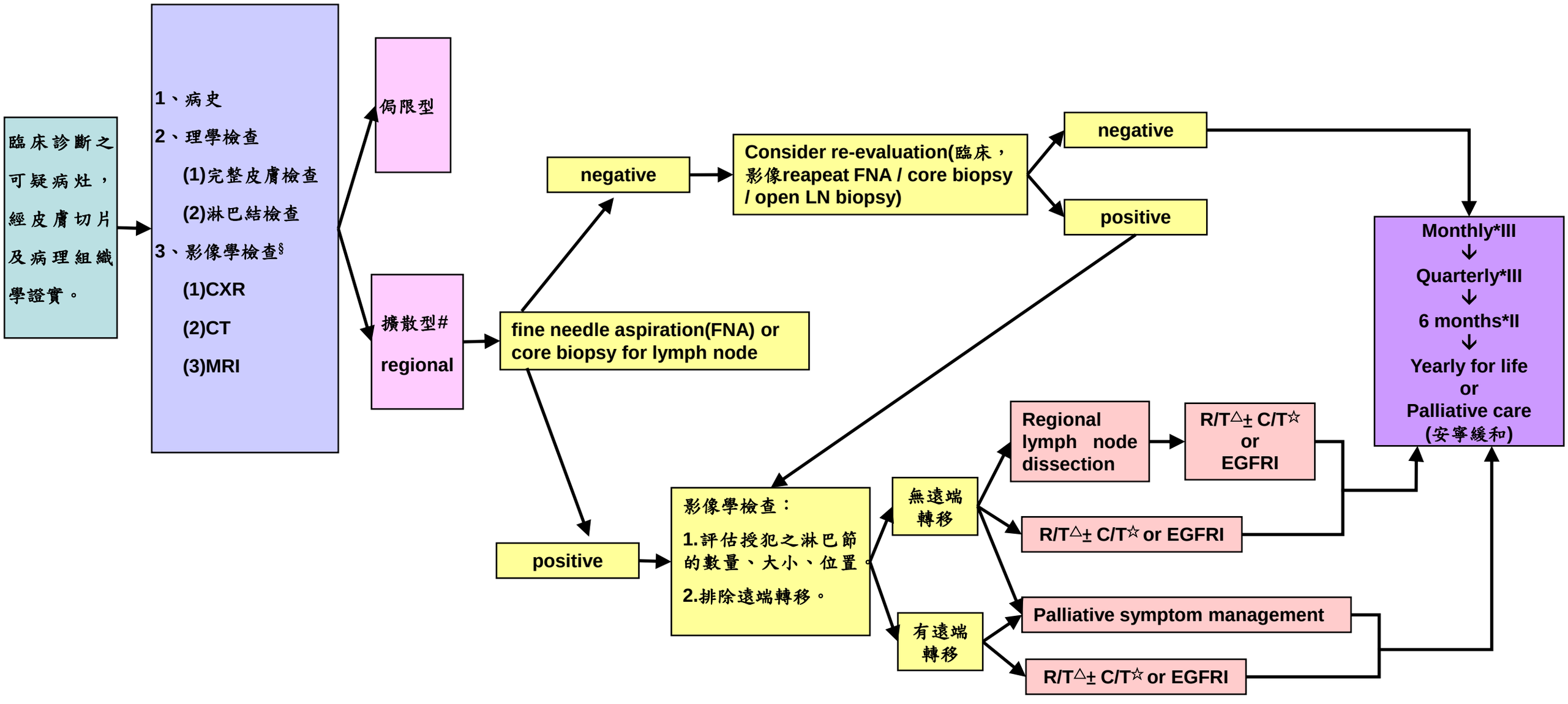
診斷	初步評估	分期	再評估(針對淋巴結)	初步治療	輔助治療	追蹤



§：Image studies is indicated for extensive disease (deep structural involvement such as bone, deep soft tissue, perineural disease)
if perineural disease is suspected, MRI is preferred.

¥： Palliative symptom management, including salvage C/T

△： RT主要針對手術不適用之情形, 附件二

＃：Palpable regional lymph node(s) or abnormal lymph nodes identified by image studies. (擴散型的“初始皮膚病灶”治療同侷限型中high risk)
T any, N1, M0 or M1 (附件三)

☆： chemotherapy regimen & EGFRI, 附件四

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復發

1、病史
2、理學檢查
(1)完整皮膚檢查
(2)淋巴結檢查
3、影像學檢查
(1)CXR
(2)CT
(3)MRI

侷限型 Local

- curettage & electrodesiccation
- wide excision
  - margin positive
    - Moh's surgery
    - RT
  - margin negative
- Moh's surgery
  - margin positive
    - RT
  - margin negative
- RT if not OP

擴散型 regional

- negative
  - Consider re-evaluation(臨床，影像reapeat FNA / core biopsy / open LN biopsy)
    - negative
    - positive
- fine needle aspiration(FNA) or core biopsy for lymph node
- positive
  - 影像學檢查：
    1.評估授犯之淋巴節的數量、大小、位置。
    2.排除遠端轉移。
    - 無遠端轉移
      - Regional lymph node dissection
        - R/T ± C/T or EGFRI
      - R/T ± C/T or EGFRI
      - Palliative symptom management
    - 有遠端轉移
      - Palliative symptom management
      - R/T ± C/T or EGFRI

Monthly*III
↓
Quarterly
or
Palliative care
(安寧緩和)

鱗狀上皮細胞癌(SCC)_ regional disease

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附件一：

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2018
Squamous Cell Skin Cancer

NCCN Guidelines Index
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RISK FACTORS FOR LOCAL RECURRENCE OR METASTASES

	Low Risk	High Risk
H&P		
Location/size[1]	Area L <20 mm Area M <10 mm[4]	Area L ≥20 mm Area M ≥10 mm Area H[5]
Borders	Well-defined	Poorly defined
Primary vs. recurrent	Primary	Recurrent
Immunosuppression	(-)	(+)
Site of prior RT or chronic inflammatory process	(-)	(+)
Rapidly growing tumor	(-)	(+)
Neurologic symptoms	(-)	(+)
Pathology		
Degree of differentiation	Well or moderately differentiated	Poorly differentiated
Acantholytic (adenoid), adenosquamous (showing mucin production), desmoplastic, or metaplastic (carcinosarcomatous) subtypes	(-)	(+)
Depth[2,3]: Thickness or Clark level	<2 mm or I, II, III	≥2 mm or IV, V
Perineural, lymphatic, or vascular involvement	(-)	(+)

Area H = "mask areas" of face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermilion], chin, mandible, preauricular and postauricular skin/sulci, temple, ear), genitalia, hands, and feet.
Area M = cheeks, forehead, scalp, neck, and pretibia.
Area L = trunk and extremities (excluding pretibia, hands, feet, nail units, and ankles).

[1]Must include peripheral rim of erythema.
[2]If clinical evaluation of incisional biopsy suggests that microstaging is inadequate, consider narrow margin excisional biopsy.
[3]A modified Breslow measurement should exclude parakeratosis or scale crust, and should be made from base of ulcer if present.
[4]Location independent of size may constitute high risk.
[5]Area H constitutes high risk based on location, independent of size. Narrow excision margins due to anatomic and functional constraints are associated with increased recurrence rates with standard histologic processing. Complete margin assessment such as with Mohs micrographic surgery is recommended for optimal tumor clearance and maximal tissue conservation. For tumors <6 mm in size, without other high-risk features, other treatment modalities may be considered if at least 4-mm clinically tumor-free margins can be obtained without significant anatomic or functional distortions.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

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附件二:

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2018
Squamous Cell Skin Cancer

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PRINCIPLES OF RADIATION THERAPY FOR SQUAMOUS CELL SKIN CANCER

Primary Tumor	Dose Time Fractionation Schedule
Definitive RT	**Examples of Dose Fractionation and Treatment Duration**
Tumor diameter <2 cm	60–64 Gy over 6 to 7 weeks 50–55 Gy over 3 to 4 weeks 40 Gy in 2 weeks 30 Gy in 5 fractions over 2 to 3 weeks
Tumor diameter ≥2 cm, T3/T4, or those with invasion of bone or deep tissue	60–70 Gy over 6 to 7 weeks 45–55 Gy over 3 to 4 weeks
Postoperative adjuvant	60–64 Gy over 6 to 7 weeks 50 Gy over 4 weeks
Regional Disease	
• Lymph node regions, after lymph node dissection	
▸ Negative margins, no ECE	50–60 Gy in 5 to 6 weeks
▸ Positive margins or ECE	60–66 Gy in 6 to 7 weeks
• Lymph node regions, without lymph node dissection	
▸ Clinically negative, at risk	50 Gy over 5 weeks
▸ Clinically positive	60–70 Gy over 6 to 7 weeks
• Clinically at-risk nerves	50–60 Gy in 5 to 6 weeks

ECE = Extracapsular extension

- Protracted fractionation is associated with improved cosmetic results and should be utilized for poorly vascularized or cartilaginous areas.
- For extensive perineural invasion, clinically evident perineural involvement, or involvement of named nerves, (particularly in the head and neck region): consider including the course of the local nerves proximally.
- Radiation therapy is contraindicated in genetic conditions predisposing to skin cancer (eg, basal cell nevus syndrome) and relatively contraindicated for patients with connective tissue diseases (eg, scleroderma).
- Given higher complication rates, re-irradiation should not be routinely utilized for recurrent disease within a prior radiation field.
- There are insufficient long-term efficacy and safety data to support the routine use of electronic surface brachytherapy.
- Radioisotope brachytherapy could be considered in highly selected cases.

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Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

鱗狀上皮細胞癌(SCC)_ regional disease

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附件三-1:

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2018 Staging Squamous Cell Skin Cancer

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Staging

American Joint Committee on Cancer (AJCC)
TNM Staging Classification for Cutaneous Squamous Cell Carcinoma of the Head and Neck (cSCC) (8th ed., 2016)

Primary Tumor (T)

TX	Primary tumor cannot be assessed
Tis	Carcinoma *in situ*
T1	Tumor smaller than 2 cm in greatest dimension
T2	Tumor 2 cm or larger, but smaller than 4 cm in greatest dimension
T3	Tumor 4 cm or larger in maximum dimension or minor bone erosion or perineural invasion or deep invasion*
T4	Tumor with gross cortical bone/marrow, skull base invasion and/or skull base foramen invasion
T4a	Tumor with gross cortical bone/marrow invasion
T4b	Tumor with skull base invasion and/or skull base foramen involvement

*Deep invasion is defined as invasion beyond the subcutaneous fat or >6 mm (as measured from the granular layer of adjacent normal epidermis to the base of the tumor); perineural invasion for T3 classification is defined as tumor cells within the nerve sheath of a nerve lying deeper than the dermis or measuring 0.1 mm or larger in caliber, or presenting with clinical or radiographic involvement of named nerves without skull base invasion or transgression.

Regional Lymph Node (N)

Clinical N (cN)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(−)
N2	Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(−); or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(−); or in metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(−)
N2a	Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(−)
N2b	Metastasis in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(−)
N2c	Metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(−)
N3	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−); or metastasis in any node(s) and clinically overt ENE [ENE(+)]
N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−)
N3b	Metastasis in any node(s) and ENE (+)

Note: A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological extranodal extension (ENE) should be recorded as ENE(−) or ENE(+).

The 8th Edition Cancer Staging System will be implemented on January 1, 2018.
For the AJCC 7th Edition Staging Manual, visit www.springer.com.

Continued

鱗狀上皮細胞癌(SCC)_ regional disease

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臨床診療指引 2018第一版

附件三-2:

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2018 Staging Squamous Cell Skin Cancer

NCCN Guidelines Index
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Discussion

Staging continued

American Joint Committee on Cancer (AJCC)
TNM Staging Classification for Cutaneous Squamous Cell Carcinoma of the Head and Neck (cSCC) (8th ed., 2016)

Regional Lymph Node (N) continued

Pathological N (pN)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(−)
N2	Metastasis in a single ipsilateral lymph node, 3 cm or smaller in greatest dimension and ENE(+); or larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(−); or metastases in multiple ipsilateral lymph nodes, none larger than 6 cm in greatest dimension and ENE(−); or in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension, ENE(−)
N2a	Metastasis in single ipsilateral node 3 cm or smaller in greatest dimension and ENE(+); or a single ipsilateral node larger than 3 cm but not larger than 6 cm in greatest dimension and ENE(−)
N2b	Metastasis in multiple ipsilateral nodes, none larger than 6 cm in greatest dimension and ENE(−)
N2c	Metastasis in bilateral or contralateral lymph node(s), none larger than 6 cm in greatest dimension and ENE(−)
N3	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−); or in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); or multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+); or a single contralateral node of any size and ENE(+)
N3a	Metastasis in a lymph node larger than 6 cm in greatest dimension and ENE(−)
N3b	Metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE(+); or multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+); or a single contralateral node of any size and ENE(+)
Note: A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L). Similarly, clinical and pathological extranodal extension (ENE) should be recorded as ENE(−) or ENE(+).	

Distant Metastasis (M)

M0	No distant metastasis
M1	Distant metastasis

AJCC Prognostic Stage Groups

Tis	N0	M0	0
T1	N0	M0	I
T2	N0	M0	II
T3	N0	M0	III
T1	N1	M0	III
T2	N1	M0	III
T3	N1	M0	III
T1	N2	M0	IV
T2	N2	M0	IV
T3	N2	M0	IV
Any T	N3	M0	IV
T4	Any N	M0	IV
Any T	Any N	M1	IV

HISTOLOGIC GRADE (G)

GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

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For the AJCC 7th Edition Staging Manual, visit www.springer.com.

附件四-1:chemotherapy regimen or metastasis

化學治療處方	
chemotherapy regimen	
published C/T regimens	**schedule**
Cisplatin, 100 mg/m2 IV D1	**Q 21-28 days x 4 cycles**
5-FU, 1 g/m2 IV D1–3	**Q 21-28 days x 4 cycles**

附件四-2:chemotherapy regimen & EGFRI or metastasis

化學治療處方

chemotherapy regimen & EGFRI	
published C/T regimens	**schedule**
Cisplatin 100 mg/m2 IV D1	**Q 21 days * 6 cycles**
5-FU 1 g/m2 IV D1-4	**Q 21 days * 6 cycles**
*** Cetuximab 400 mg/m2 ; 250 mg/m2 IV**	**400 mg/m2 * Week 1；then 250 mg/m2 * QW**

* Cetuximab could be continued as long as the response or the stabilization persisted

附件四-2:chemotherapy regimen & EGFRI or metastasis

化學治療處方	
chemotherapy regimen & EGFRI	
published C/T regimens	**schedule**
Cisplatin 100 mg/m2 IV D1	**Q 21 days * 6 cycles**
5-FU 1 g/m2 IV D1-4	**Q 21 days * 6 cycles**
•Cetuximab, 400 mg/m2 IV Week 1, then 250 mg/m2 QW	**Till IV or unacceptable toxicity**

* Cetuximab could be continued as long as the response or the stabilization persisted

附件四-3:EGFRI or metastasis

化學治療處方	
EGFRI	
published C/T regimens	**schedule**
•Cetuximab, 400 mg/m2 IV Week 1, then 250 mg/m2 QW	**Till IV or unacceptable toxicity**

* Cetuximab could be continued as long as the response or the stabilization persisted

Reference

1. NCCN Clinical Practice Guideline in Oncology, Basal and Squamous Cell Skin Cancers, Version 2.2018
2. Am J Clin Dermatol. 2016 Oct;17(5):491-508. Cutaneous Squamous Cell Carcinoma: A Review of High-Risk and Metastatic Disease.
3. Mendenhall WM, Ferlito A, Takes RP, et al. Cutaneous head and neck basal and squamous cell carcinomas with perineural invasion. Oral Oncol 2012;48:918-922.
4. Gurudutt VV, Genden EM. Cutaneous squamous cell carcinoma of the head and neck. J Skin Cancer 2011;2011:502723.
5. Phase II study of cetuximab as first-line single-drug therapy in patients with unresectable squamous cell carcinoma of the skin. J Clin Oncol. 2011 Sep 1;29(25):3419-26
6. Lott DG, Manz R, Koch C, Lorenz RR. Aggressive behavior of nonmelanotic skin cancers in solid organ transplant recipients. Transplantation 2010;90:683-687.
7. Cranmer LD, Engelhardt C, Morgan SS. Treatment of unresectable and metastatic cutaneous squamous cell carcinoma. Oncologist 2010;15:1320-1328.
8. Brantsch KD, Meisner C, Schonfisch B, et al. Analysis of risk factors determining prognosis of cutaneous squamous-cell carcinoma: a prospective study. Lancet Oncol 2008;9:713-720.
9. Platinum-Based Chemotherapy plus Cetuximab in Head and Neck Cancer.N Engl J Med 2008;359:1116-27.Neville JA, Welch E, Leffell DJ.Management of nonmelanoma skin cancer in 2007. Nat Clin Pract Oncol 2007;4:462-469.
10. Squamous cell carcinoma developing on burn scar. Ann Plast Surg 2006;56:406-408.
11. Ross AS, Schmults CD. Sentinel lymph node biopsy in cutaneous squamous cell carcinoma: a systematic review of the English literature. Dermatol Surg 2006;32:1309-1321.
12. Veness MJ, Morgan GJ, Palme CE, Gebski V. Surgery and adjuvant radiotherapy in patients with cutaneous head and neck squamous cell carcinoma metastatic to lymph nodes: combined treatment should be considered best practice. Laryngoscope 2005;115:870-875.