



# 振興醫療財團法人振興醫院

Cheng Hsin General Hospital

甲狀腺癌診療指引

*Thyroid cancer Guideline*

2016/07 訂定

2017/12/04 修訂

# 多專科團隊成員

- 腫瘤內科
- 腫瘤外科
- 放射診斷科
- 病理科
- 核子醫學科
- 放射治療科
- 癌症個管師
- 社工/心理師
- 營養師

## 治療前檢查

- 病史及身體評估
- 甲狀腺功能檢查
- 甲狀腺相關自體抗體檢查
- 甲狀腺超音波檢查
- 甲狀腺切片檢查 (FNAC/FNAB)
  - 其他影像檢查
    - 頸部電腦斷層
    - 核醫影像檢查
    - 頸部核磁共振檢查
    - 正子攝影 (PET/CT)

## 第一線檢查包括：

- 檢測**TSH**數值
- 如**TSH**數值低下，建議做甲狀腺核子醫學掃描
- 亢進性結節極少為惡性

Boelaert K et al. JCEM 2006; 91:4295 - 4301.

## 必須要做哪些影像檢查？

- 有甲狀腺結節病患要做甲狀腺超音波檢查
- 超音波檢查是最有用的影像檢查
- 用來評估甲狀腺結節形狀與大小，  
並做甲狀腺抽吸與追蹤

Cooper DS, et al. Thyroid 2009; 19: 1167-1214

# 細胞學種類

- 惡性 (malignant) (95%以上機率為惡性): 手術切除。
- 疑似為惡性 (suspicious for malignancy) (50% - 75%機率為惡性)： 強烈建議手術切除。
- 濾泡型 (follicular) 或嗜酸細胞瘤 (hurthle cell neoplasm) (約有20-30%為惡性): 建議手術切除。  
。
- 臨床意義未明之濾泡病灶 (Follicular lesion of undetermined significance) (約5 - 10%為惡性)；通常無法區別是良性或濾泡型腫瘤；此類病人可受惠於反覆細針抽吸，並且與臨床或影像檢查做對照。
- 良性病灶 (Benign lesions)： 應每6-12個月追蹤超音波，；若結節變大且為1公分以上或形態高度懷疑惡性，才建議重作細針抽吸；若體積增加50%則認定為結節有意義的變大。
- 無法診斷 (Nondiagnostic) (經由手術切除後，約5 - 10%為惡性): 建議病灶大於1公分時重複做細針抽吸才建議密切追蹤或直接開刀移除

\*如腫瘤大於3公分，建議手術切除；尤其是年輕病人

Baloch ZW, et al. Diagnostic Cytopathology; 2008; 36: 425-437  
Cooper DS, et al. Thyroid 2009; 19: 1167-1214  
McCoy KL, et al. Surgery. 2007;142:837-844.

## 超音波特徵

### 實質結節

- 具有懷疑為惡性的甲狀腺特徵 > 1.0 公分以上
- 缺乏疑似惡性的甲狀腺特徵 >1.5公分以上

### 混合實體與囊樣的結節

- 具有懷疑為惡性的甲狀腺特徵 >1.5-2.0公分以上
- 缺乏疑似惡性的甲狀腺特徵 >2.0公分以上

### 海綿樣結節

>2.0公分以上

### 單純囊樣

不需要

### 疑似頸部淋巴結轉移

淋巴結抽吸 +/- 甲狀腺結節抽吸

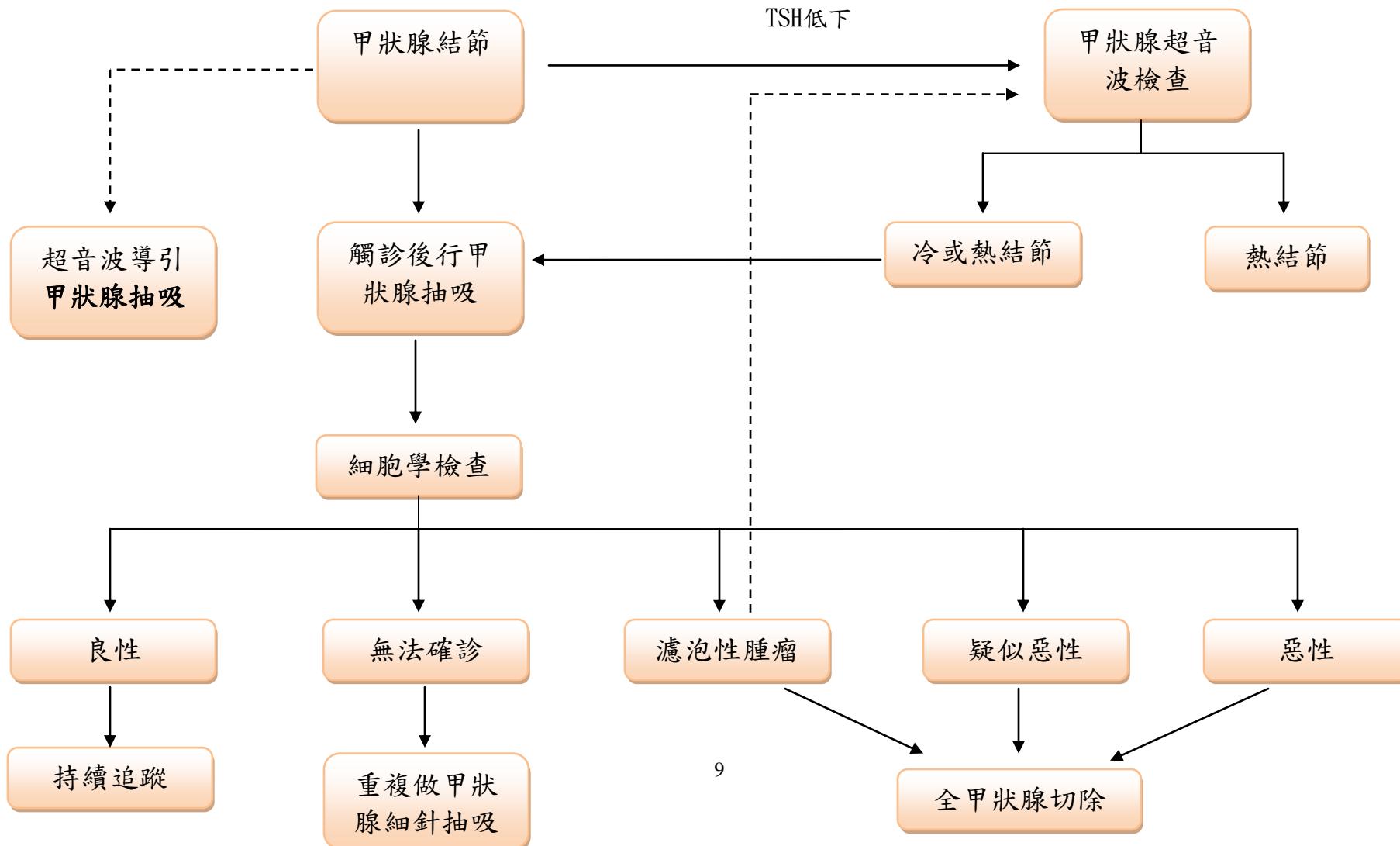
上述標準是通用準則，若患者具有高風險的臨床特徵時，結節雖小於上述閾值，醫師臨牀上認定需要抽吸檢測也被認為是合乎常規的。經過完整告知的患者，若具有高風險臨床特徵或4公分以上的結節時，也可以選擇直接進行甲狀腺全葉切除或甲狀腺全切除，來獲得確定的組織學診斷。

# 疑似為惡性可以進一步分為下列幾種：

- 疑似乳突狀甲狀腺癌(papillary carcinoma)
- 疑似甲狀腺髓樣癌(medullary carcinoma)
- 懷疑為其他惡性腫瘤：  
淋巴瘤(lymphoma)或轉移至甲狀腺的腫瘤(metastatic)
- 完全都是壞死細胞，疑似為惡性 (Suspicious for neoplasm because of total necrosis of lesional cells) [如：未分化癌(anaplastic carcinoma)]

Baloch ZW, et al. Diagnostic Cytopathology; 2008; 36: 425–437

## 甲狀腺結節檢查順序



## 組織病理學型態

- 分化良好之濾泡型甲狀腺癌
  - 甲狀腺乳突癌 (Papillary thyroid carcinoma)
  - 甲狀腺濾泡癌 (Follicular thyroid carcinoma)
- 分化不良甲狀腺癌 (Poorly differentiated thyroid carcinoma)
- 未分化甲狀腺癌 [Anaplastic (undifferentiated) thyroid carcinoma]
- 非濾泡性甲狀腺癌(Non-follicular thyroid carcinoma)
- 甲狀腺髓樣癌 (Medullary thyroid carcinoma)
- 其他
  - 淋巴癌 (lymphoma)
  - 轉移到甲狀腺的癌症 (metastasis to thyroid)
  - 無法區分癌細胞型態 (Carcinoma, type cannot be determined)
  - 無法確定惡性度之濾泡樣腫塊 (Follicular neoplasm of uncertain malignant potential)

## 與治療相關的簡稱

- 人類甲狀腺球蛋白(Human thyroglobulin): hTg
- 手術流程 (Operation procedures)
  - 甲狀腺切除術 (Thyroidectomy): Tx
  - 甲狀腺次全切除術 (Subtotal thyroidectomy): sTx
  - 甲狀腺全切除術 (Total thyroidectomy): TTx
  - 中央淋巴結廓清術 (Central lymph node dissection): CLND
  - 改良型根治性淋巴結廓清術 (Modified radical lymph node dissection): MRLND
- 碘131治療 (Radioiodine): RAI
- 體外放射治療 (External-beam radiation therapy): EBRT
- 副甲狀腺切除術 (Parathyroidectomy): PTX

# 甲狀腺乳突癌 (PTC)

細針抽吸發現PTC

- 甲狀腺超音波
- 較嚴重案例可作電腦斷層或核磁共振
- 考慮評估聲帶功能
- 胸部 X 光

## 全切除術(TTx)的適應症：

1. 惡性度較高之分型
2. 曾接受過放射線治療
3. 已知有遠端轉移
4. 侵犯至甲狀腺外
5. 肿瘤直徑超過4公分
6. 頸部淋巴結轉移
7. 惡性度較高之分型

## 全切除術(TTx)

1. 當可觸摸到淋巴結或淋巴切片呈陽性
  - 中央淋巴結廓清術(CLND)
  - 頸側淋巴廓清術
2. 淋巴結為陰性但腫瘤極為惡性
  - 可考慮預防性中央淋巴結廓清術

## 全切除術(TTx) 或甲狀腺切除術(Tx)

1. 不曾接受放射線
2. 無遠端轉移
3. 無甲狀腺外侵犯
4. 肿瘤小於 4 公分
5. 無頸部淋巴結轉移
6. 非惡性度較高之分型

## 全切除術(TTx)

或

## 甲狀腺切除術

以下情況

- 肿瘤大於4公分
- 手術邊緣有殘留癌細胞
- 肿瘤已向外擴展
- 巨觀下有多處病灶
- 已確定有淋巴結轉移
- 肿瘤已侵犯血管

## 甲狀腺切除術

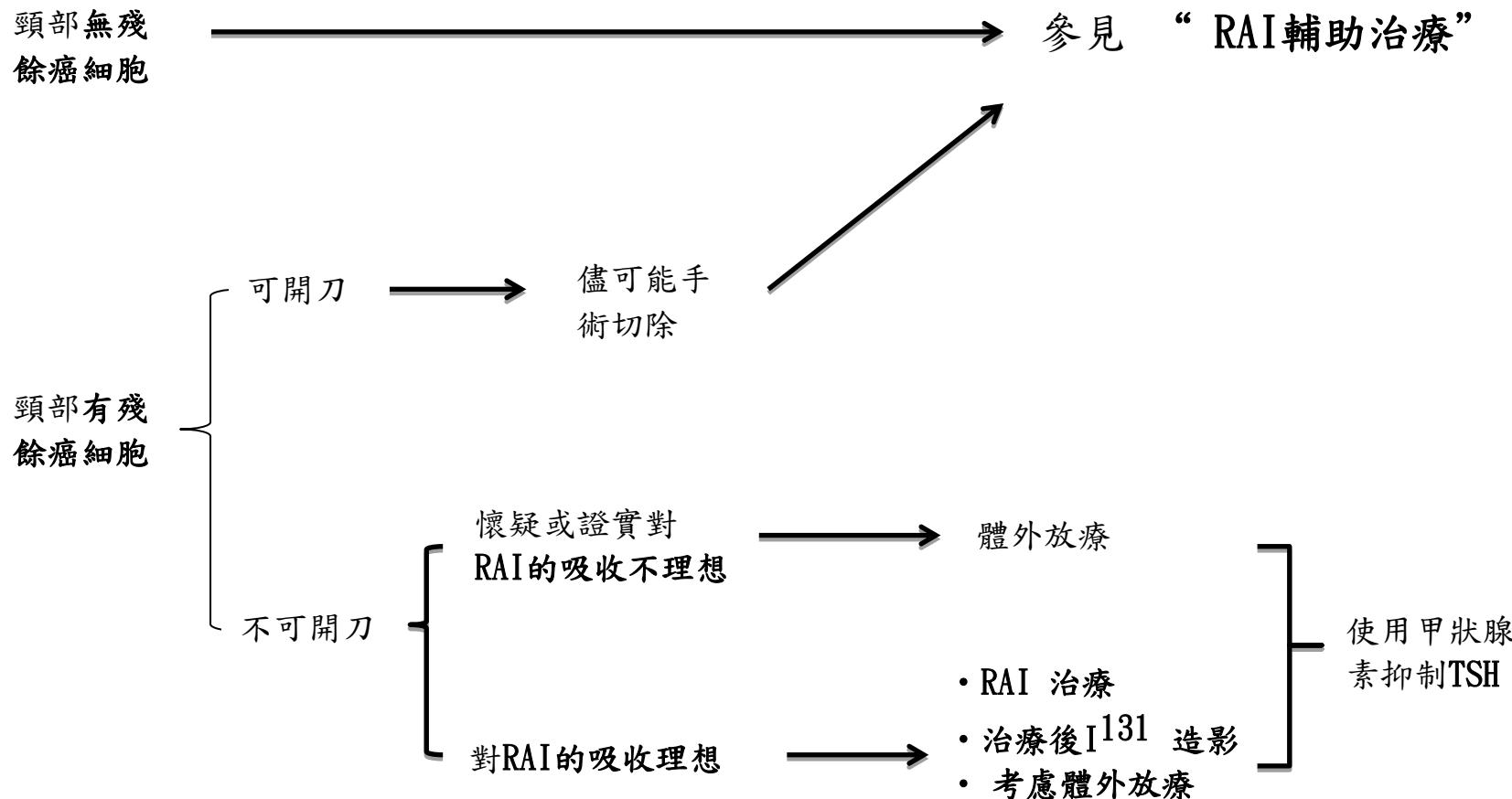
有

無

考慮

- 檢測HTG
- 使用甲狀腺素
- 治療抑制TSH數值

# 甲狀腺乳突癌 (PTC)



## RAI輔助治療 (PTC)

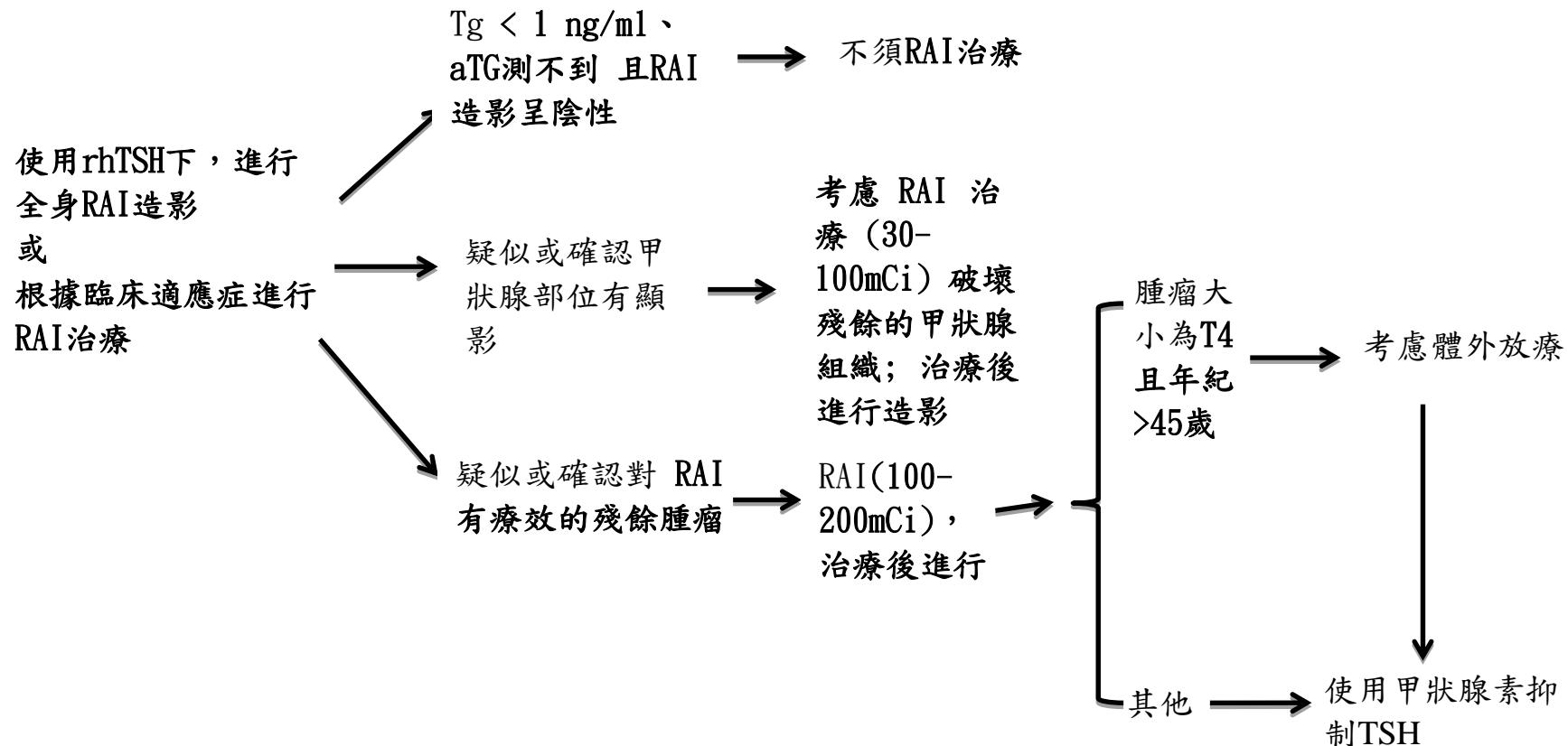
➤ 建議做 $I^{131}$  RAI 治療：

- 腫瘤已延伸至甲狀腺外
- 腫瘤大於4公分
- 確定或懷疑有遠端轉移

➤ 選擇性進行 $I^{131}$  RAI 治療：

- 懷疑手術後仍有殘留的甲狀腺組織
- 高惡性度組織型態
- 有侵犯血管
- 頸部淋巴結轉移
- 稍稍有甲狀腺外的延伸
- 術後之甲狀腺球蛋白未能如預期降低

## PTC病人術後進行RAI治療的考量

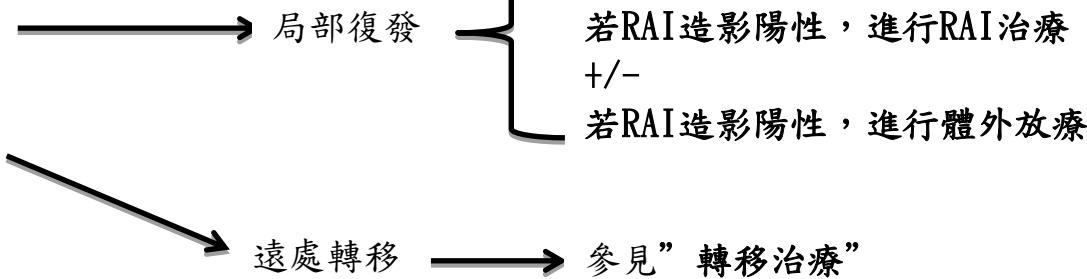


## PTC病人的追蹤

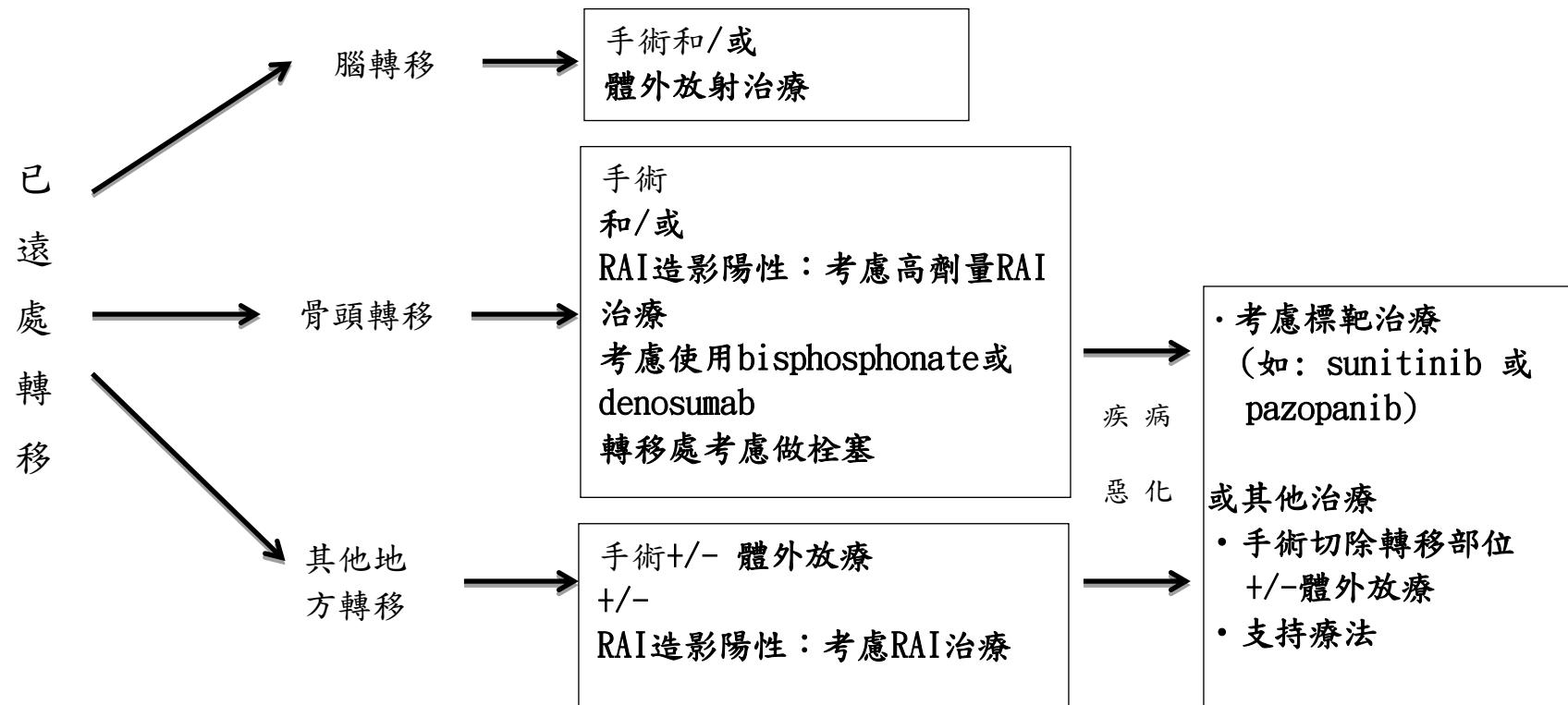
### 追蹤

- 身體檢查，檢測 TSH、Tg 和 aTG
- 頸部超音波
- 下列高風險病人，考慮進行以 TSH刺激之RAI造影：病人先前就有會吸收RAI的遠端轉移、病人的 Tg 數值異常、持續存在或逐漸升高的 aTG 數值、超音波追蹤發現異常
- 若RAI造影無異常，但 hTg 升高，應考慮使用非RAI的影像檢查，如：頸部超音波、頸部電腦斷層或胸部斷層或正子攝影

### 疾病復發

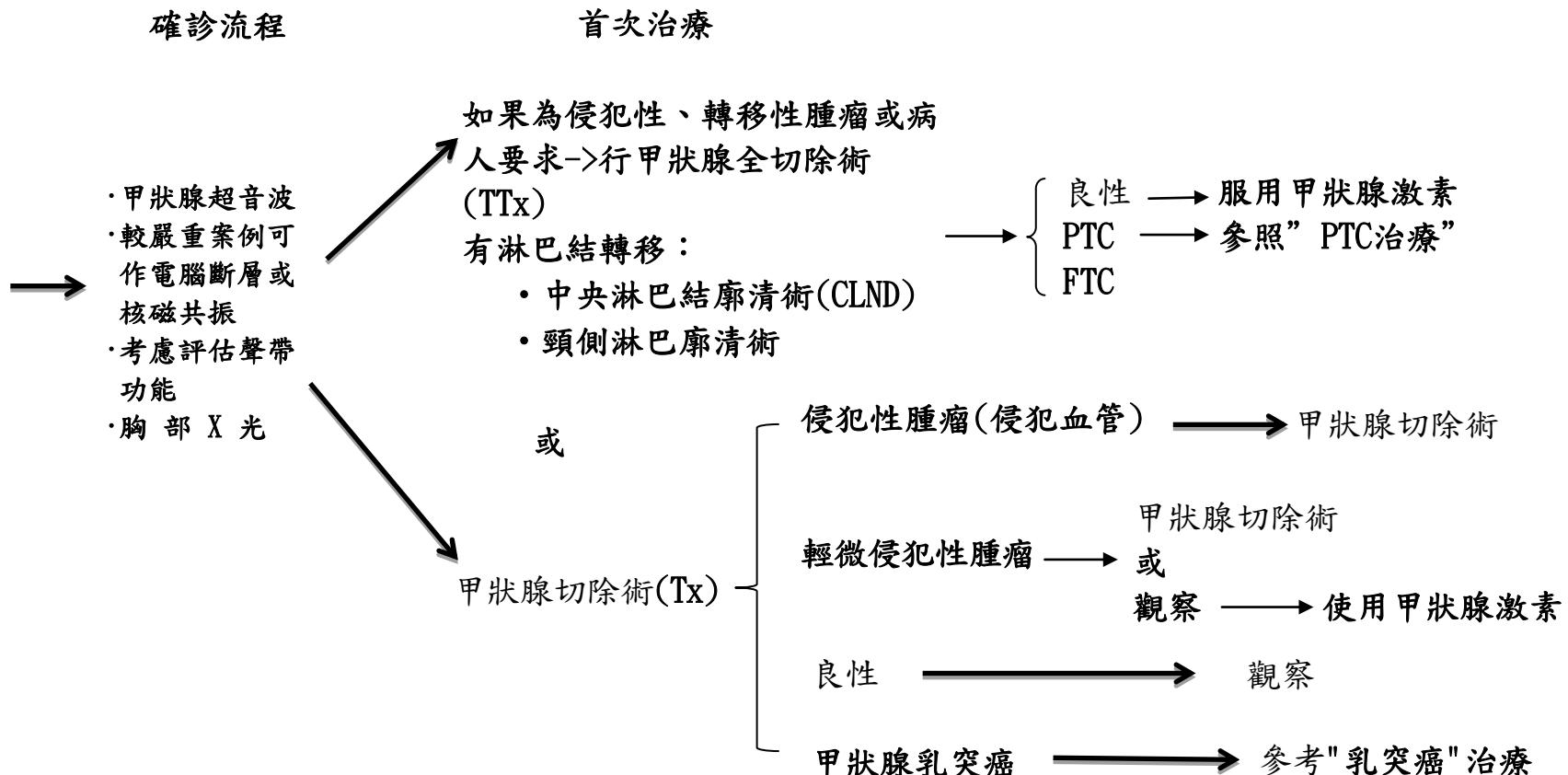


# 轉移治療(PTC)

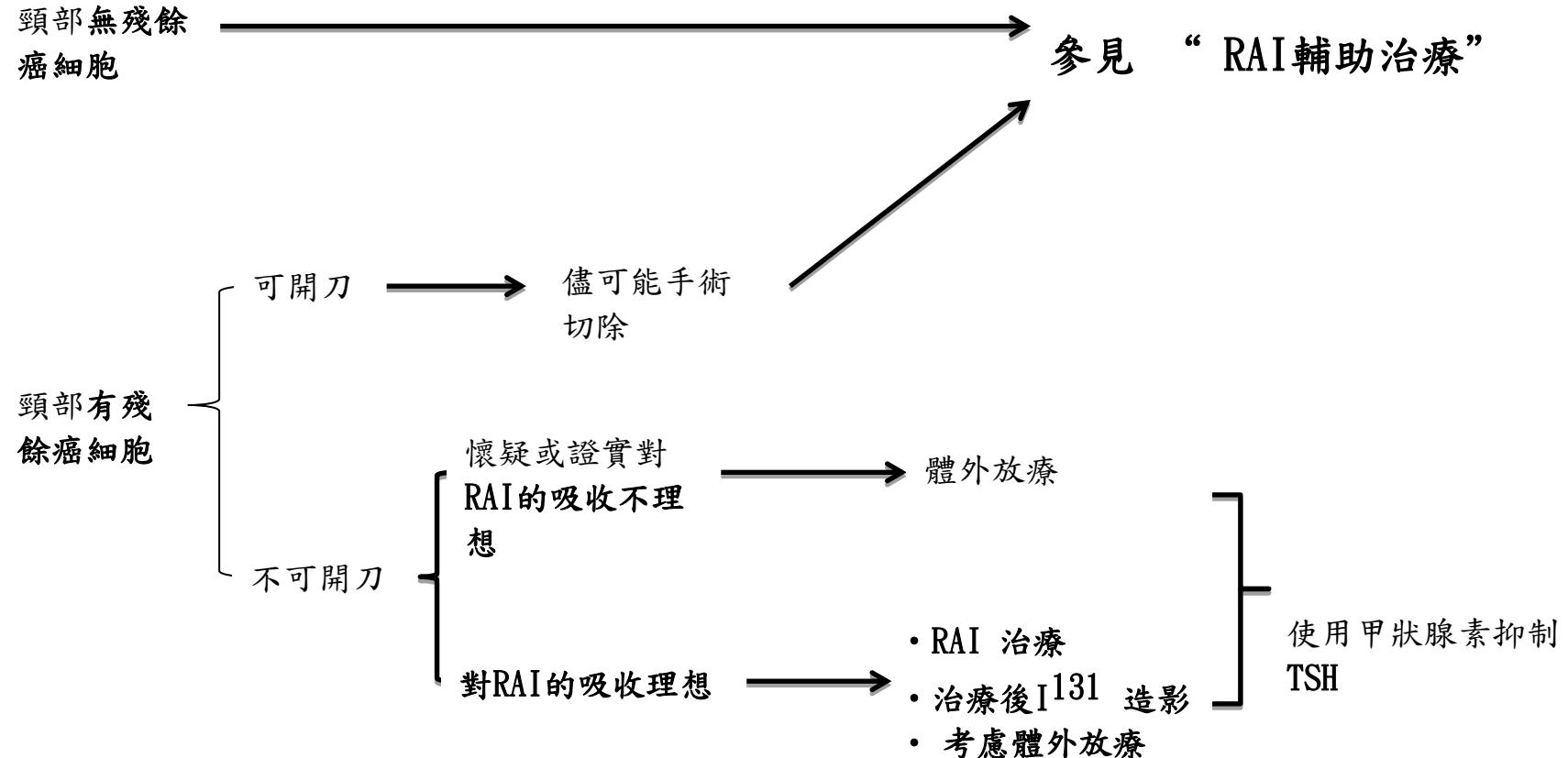


# 甲狀腺濾泡癌(FTC)

甲狀腺濾泡結節或未確診的腫結節



## 甲狀腺濾泡癌之治療 (FTC)



## RAI輔助治療 (PTC)

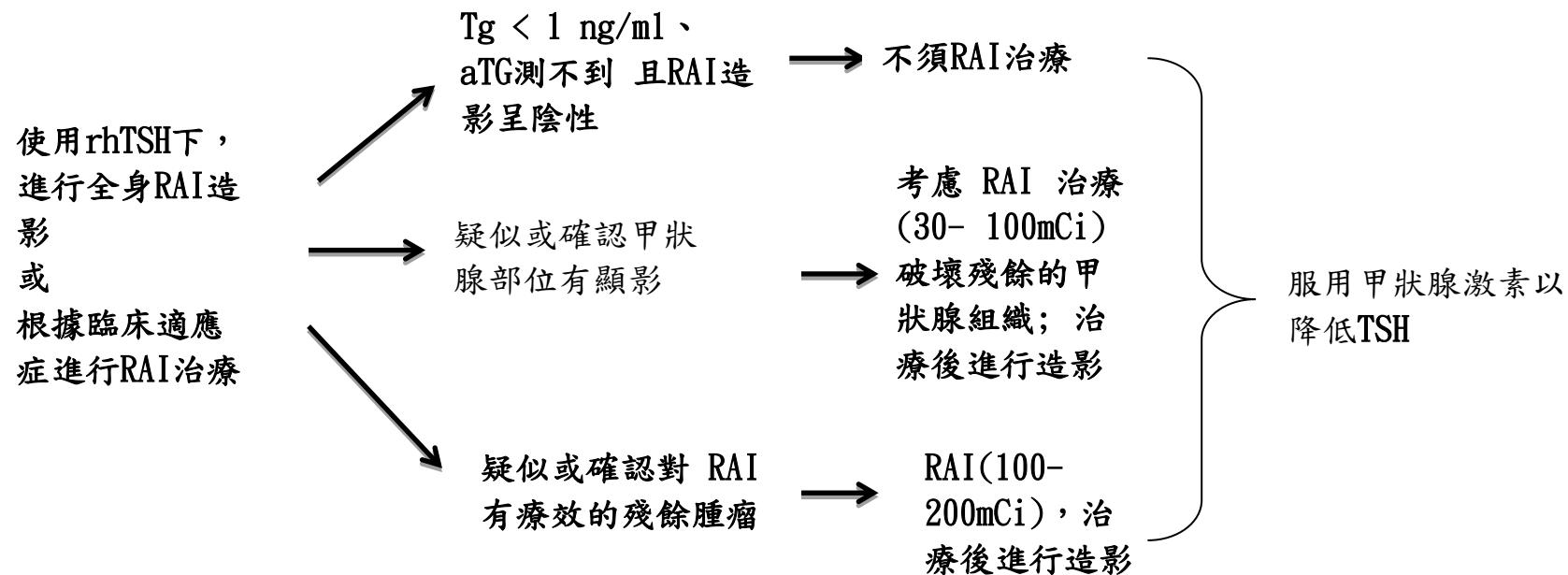
➤ 建議做 $I^{131}$  RAI 治療：

- 腫瘤已超出甲狀腺
- 原發腫瘤大於
- 懷疑遠處轉移
- 已侵犯血管

➤ 選擇性進行 $I^{131}$  RAI 治療：

- 懷疑手術後仍有殘留的甲狀腺組織
- 高惡性度組織型態
- 輕微血管侵犯血管
- 頸部淋巴結轉移
- 稍稍有甲狀腺外的延伸
- 術後之甲狀腺球蛋白未能如預期降低

## FTC病人術後進行RAI治療的考量



# FTC病人的追蹤

## 追蹤

- 身體檢查，檢測 TSH、Tg 和 aTG
- 頸部超音波
- 下列高風險病人，考慮進行以 TSH 刺激之 RAI 造影：病人先前就有會吸收 RAI 的遠端轉移、病人的 Tg 數值異常、持續存在或逐漸升高的 aTG 數值、超音波追蹤發現異常
- 若 RAI 造影無異常，但 hTg 升高，應考慮使用非 RAI 的影像檢查，如：頸部超音波、頸部電腦斷層或胸部斷層或正子攝影

## 疾病復發

→ 局部復發

若可切除，直接手術

+/-

若 RAI 造影陽性，進行 RAI 治療

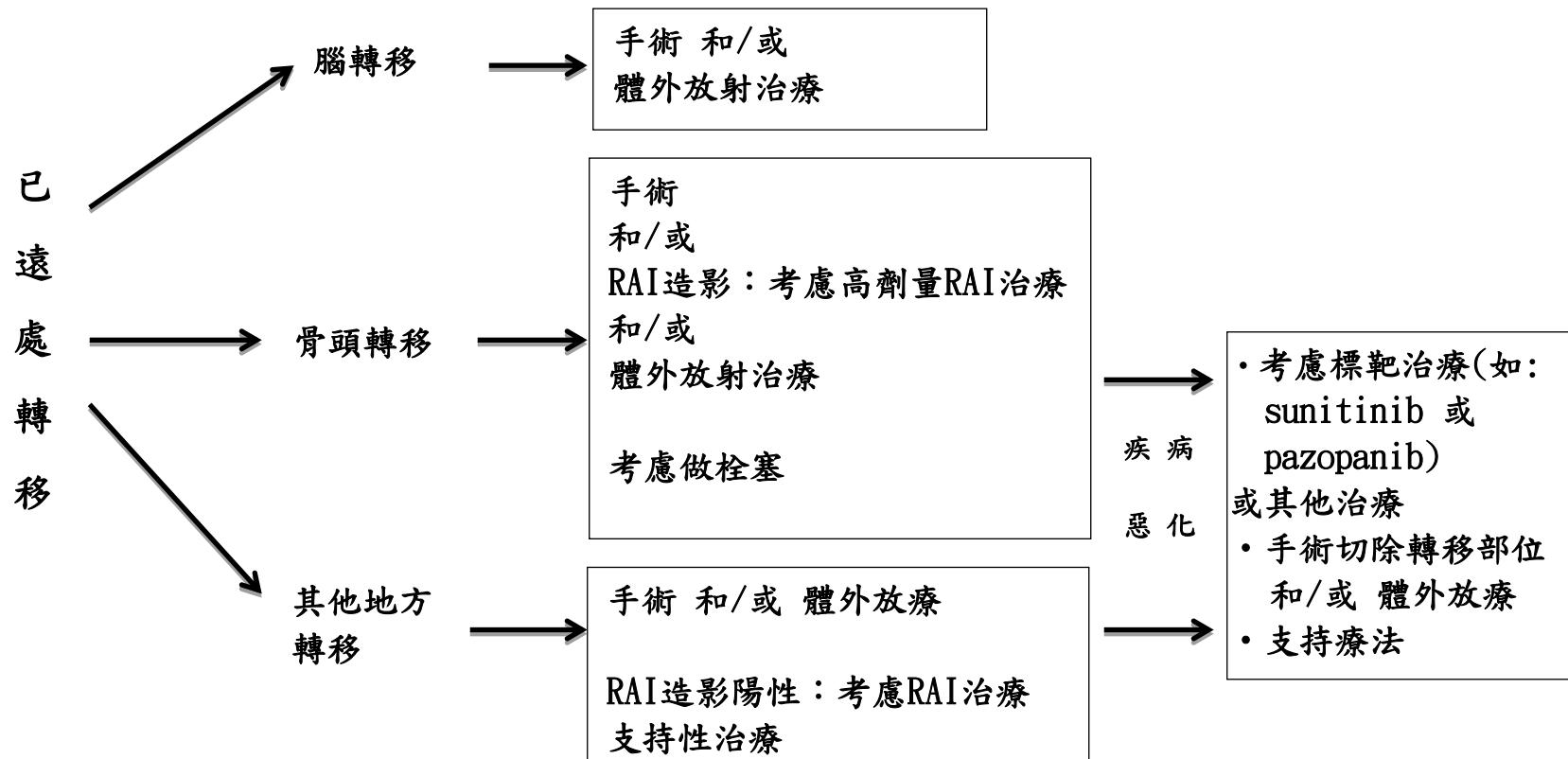
+/-

若 RAI 造影陽性，進行體外放療

→ 遠處轉移

→ 參見“轉移治療”

## FTC遠處轉移治療



# 甲狀腺髓樣癌 (MTC)

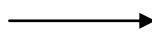
臨床表現

檢查

治療

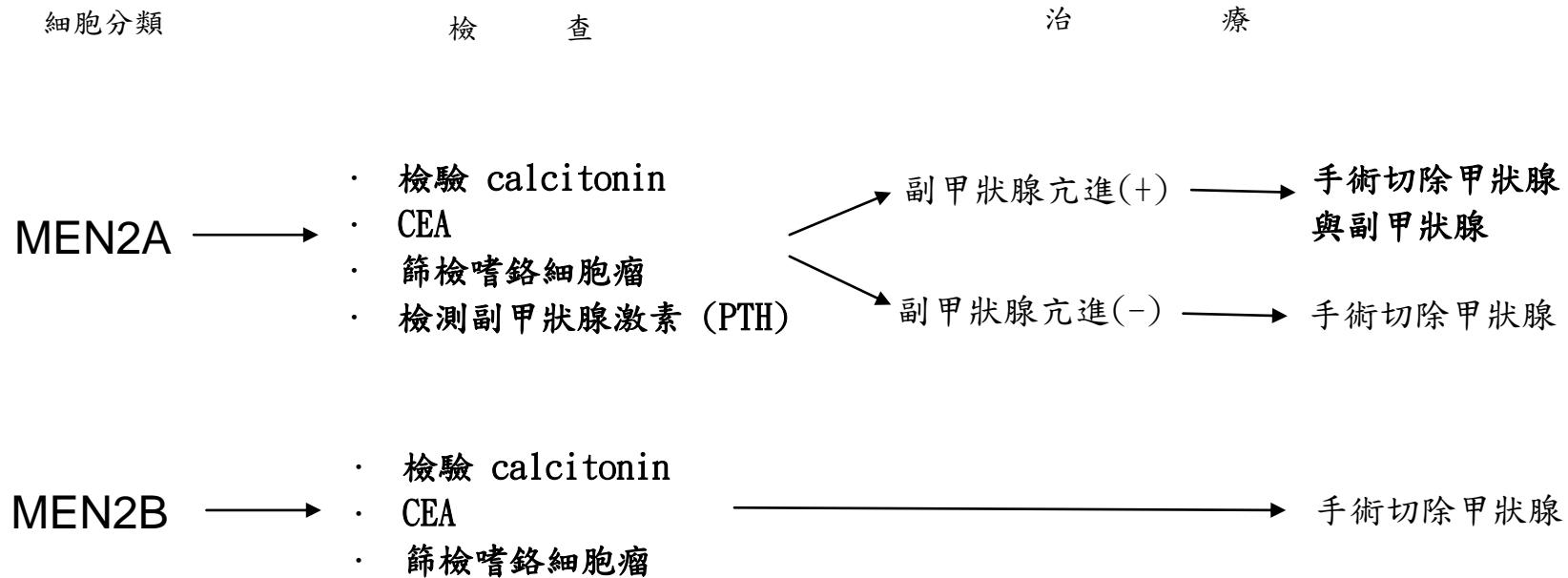
甲狀腺  
髓樣癌

- 檢驗 Calcitonin 數值
- CEA
- 篩檢嗜鉻細胞瘤
- 血鈣
- 頸部超音波
- 如有淋巴轉移或 Calcitonin > 400 pg/ml, 建議可做電腦斷層或核磁共振
- 可考慮自費檢驗 RET proto-oncogene



- 甲狀腺全切合併中央淋巴結廓清術
- 臨床或影像確定有淋巴轉移, 改良性單側或雙側淋巴結完全廓清術
- 考慮預防性單側淋巴結完全廓清術
- 對於腫瘤無法全切的病患可考慮體外放療
- 對於腫瘤擴散到甲狀腺外(T4a 或 T4b)且術後仍有殘存癌細胞的病患建議做術後體外放療
- 術後給予 levothyroxine 維持 TSH 在正常範圍

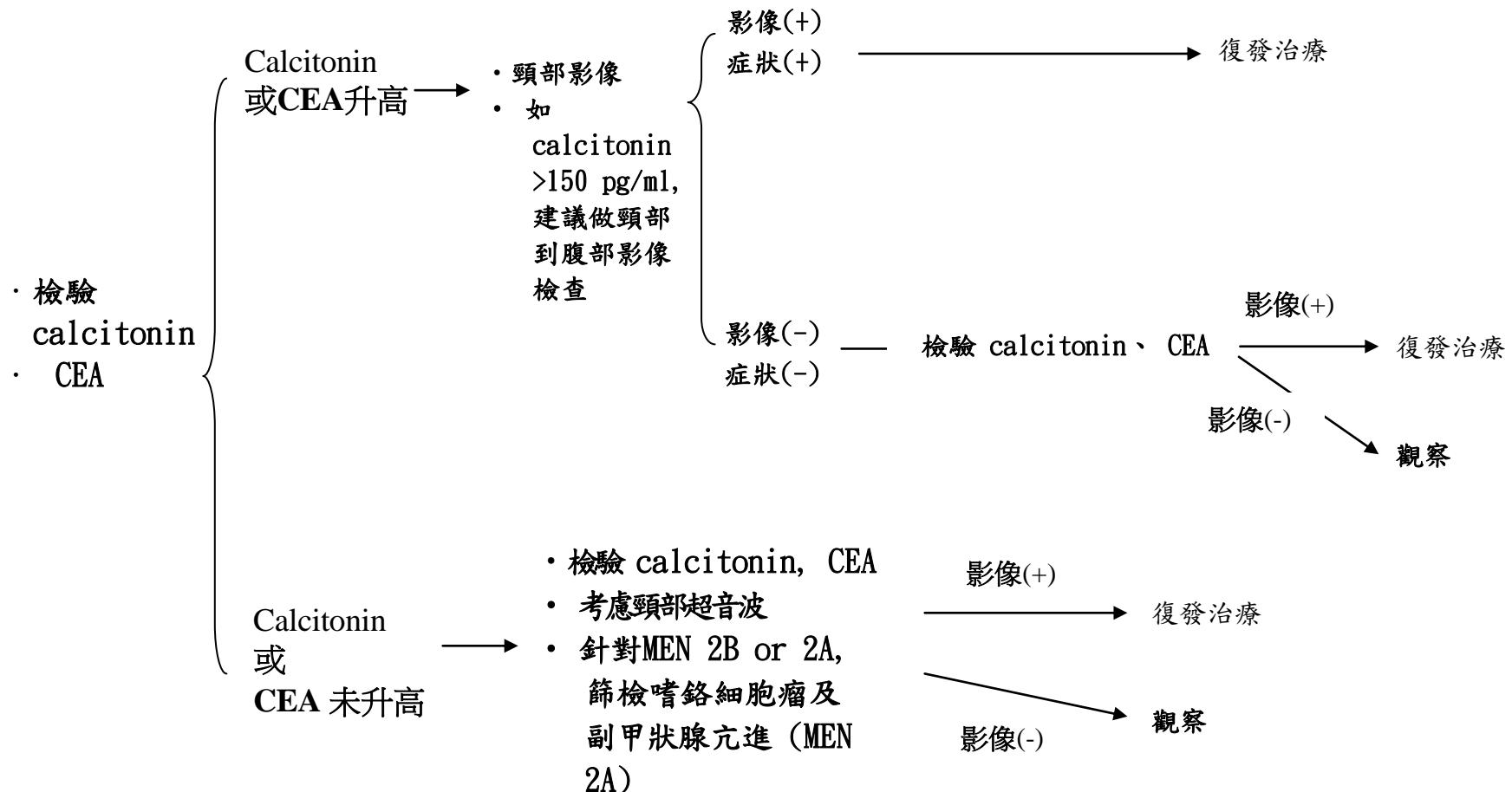
# 甲狀腺髓樣癌(MTC) 與 多發性內分泌腺瘤 (MEN)



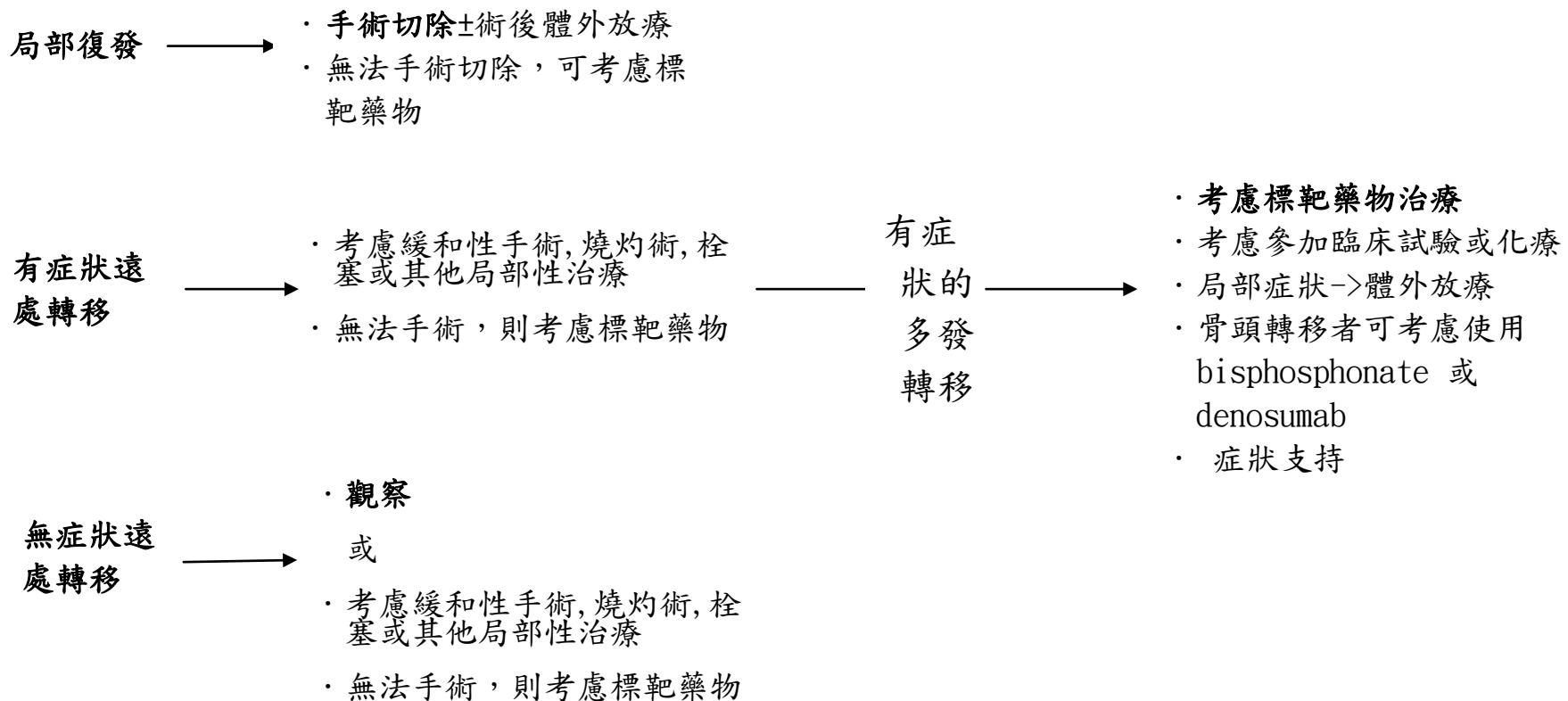
• MEN 2A : 包括有甲狀腺髓質癌和嗜鉻性細胞瘤，並且合併有副甲狀腺高能症。

• MEN 2B : 除了甲狀腺髓質癌和嗜鉻性細胞瘤外，則合併多發性黏膜神經瘤、  
Marfanoid habitus、medullary corneal nerve fibers、megacolon

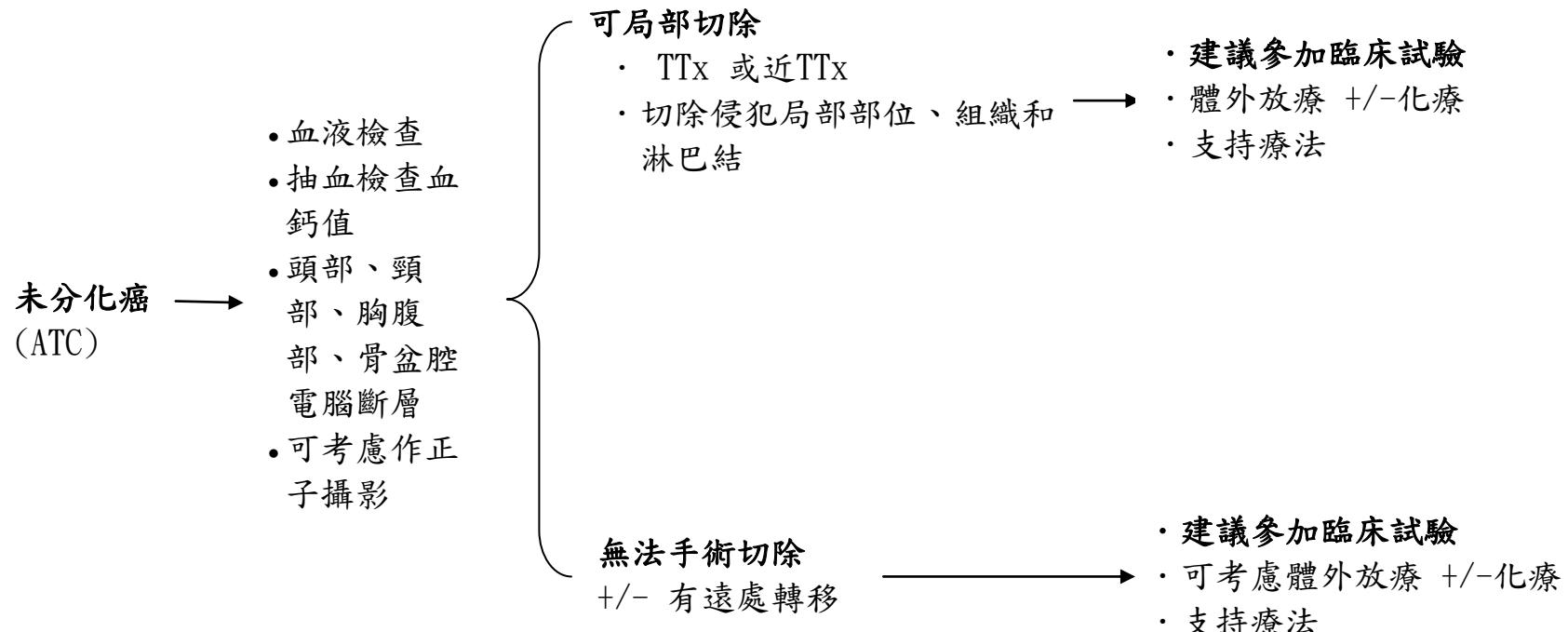
# MTC病人的追蹤與復發



## MTC持續存在或復發



# 未分化癌 (ATC)



## 甲狀腺癌分期

T : primary tumor , 原發腫瘤

|     |                                                                                        |
|-----|----------------------------------------------------------------------------------------|
| Tx  | 原發腫瘤無法評估                                                                               |
| T0  | 無原發腫瘤。                                                                                 |
| T1  | 腫瘤≤ 2 CM, 在甲狀腺包膜內。                                                                     |
| T1a | 腫瘤≤ 1 CM, 在甲狀腺包膜內                                                                      |
| T1b | 1 CM < 腫瘤≤ 2 CM, 在甲狀腺包膜內                                                               |
| T2  | 2 CM < 腫瘤≤ 4 CM, 在甲狀腺包膜內。                                                              |
| T3  | 4 CM < 腫瘤, 在甲狀腺包膜內；或腫瘤已稍微擴散至甲狀腺包膜外(minimal extrathyroid extension)例如侵犯到胸骨甲狀肌或甲狀腺周圍軟組織。 |
| T3a | 4CM>腫瘤, 在甲狀腺包膜內。                                                                       |
| T3b | 癌腫瘤侵犯至或腫瘤已稍微擴散至甲狀腺包膜外(strnohyoid、thyrohyoid, or omohyoid muscles)來自任何大小的腫瘤             |
| T4  | 包含總體外擴張                                                                                |
| T4a | 癌腫瘤侵犯至皮下軟組織、喉部 (larynx)、氣管、食道、或喉返神經                                                    |
| T4b | 癌腫瘤侵犯至脊柱前的筋膜，或包住頸動脈或縱隔腔血管                                                              |

N : regional lymph node , 區域淋巴轉移

|     |                                               |
|-----|-----------------------------------------------|
| N0  | 區域淋巴結無法評估。                                    |
| Nx  | 沒有區域淋巴結轉移。                                    |
| N1  | 區域淋巴結轉移。                                      |
| N1a | 區域淋巴結轉移至第六區 (氣管前、氣管旁、喉前/Delphian 淋巴結)。        |
| N1b | 區域淋巴結轉移至外頸部 (單側, 雙側, 對側)或咽後淋巴結或上縱隔腔(第七區) 淋巴結。 |

M : Distant metastasis , 遠端轉移

|    |         |
|----|---------|
| M0 | 沒有遠端轉移。 |
| M1 | 有遠端轉移   |

# Thyroid Carcinoma Staging

## 甲狀腺乳突癌或濾泡癌

55歲以下

Stage I Any T Any N M0

Stage II Any T Any N M1

## 甲狀腺乳突癌或濾泡癌

55歲以上

Stage I T1 N0/NX M0

Stage I T2 N0/NX M0

Stage II T1 N1 M0

Stage II T2 N1 M0

Stage II T3a/T3b AnyN M0

Stage III T4a AnyN M0

Stage IVA T4b AnyN M0

Stage IVB AnyT AnyN M1

## 髓樣癌

Stage I T1 N0 M0

Stage II T2 N0 M0

T3 N0 M0

Stage III T1 N1a M0

T2 N1a M0

T3 N1a M0

Stage IVA T4a AnyN M0

T1-3 N1b M0

Stage IVB T4b Any N M0

Stage IVC Any T Any N M1

## Anaplastic 均為第4期

Stage IVA T1-T3a N0/NX M0

Stage IVB T1-3a N1 M0

Stage IVB T3b AnyN M0

Stage IVB T4 AnyN M0

Stage IVC Any T Any N M1

## Reference

- Patel S, Shah JP. Part II: Head and neck sites. In: Edge SB, Byrd DR, Carducci MA, Compton CA, eds. *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2018.
- DeLellis RA, Lloyd RV, Heitz PU, Eng C, eds. *World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Endocrine Organs*. Lyon: IARC Press; 2004.
- Sabin LH, Wittekind C. *UICC TNM Classification of Malignant Tumours*. 6th ed. New York: Wiley-Liss; 2002.
- Rosai J, Carcangiu ML, DeLellis RA. *Atlas of Tumor Pathology. Tumors of the Thyroid Gland. 3rd series. Fascicle 5*. Washington, DC: Armed Forces Institute of Pathology; 1992.
- Chan JKC. The thyroid gland. In: Fletcher CDM, ed. *Diagnostic Histopathology of Tumours*. 3rd ed. Edinburgh; Churchill Livingstone Elsevier; 2007:1018.
- Komorowski RA, Hanson GA. Occult thyroid pathology in the young adult: an autopsy study of 138 patients without clinical thyroid disease. *Hum Pathol*. 1988;19:689-696.
- Ghossein RA, Hiltzik RA, Carlson DL, et al. Prognostic factors of recurrence in encapsulated Hürthle cell carcinoma of the thyroid gland: a clinicopathologic study of 50 cases. *Cancer*. 2006;106:1669-76.
- Stojadinovic A, Ghossein RA, Hoos A, et al. Hürthle cell carcinoma: a critical histopathologic appraisal. *J Clin Oncol*. 2001;19:2616-25.
- Collini P, Sampietro G, Pilotti S. Extensive vascular invasion is a marker of risk of relapse in encapsulated non-Hürthle cell follicular carcinoma of the thyroid gland: a clinicopathological study of 18 consecutive cases from a single institution with a 11-year median follow-up. *Histopathology*. 2004;44:35-9.
- Standring S. Thyroid gland. In: Standring S, ed. *Gray's Anatomy: The Anatomical Basis of Clinical Practice*. 39th ed. Edinburgh: Elsevier Churchill Livingstone; 2005:560-564.
- Rosai J, Carcangiu ML, DeLellis RA. The normal thyroid gland. In: Rosai J, ed. *Tumors of the Thyroid. Atlas of Tumor Pathology. Fascicle 5. Third series*. Washington, DC: Armed Forces Institute of Pathology; 1992: 1-17.
- Gnepp DR, Ogorzalek JM, Heffess CS. Fat-containing lesions of the thyroid gland. *Am J Surg Pathol*. 1989;13:605-612.
- Carcangiu ML. Thyroid. In: Mills SE, ed. *Histology for Pathologists*. Third ed. Philadelphia; Lippincott Williams & Wilkins; 2007: 1129-1148.

- Robbins KT et al. Neck dissection classification update. *Arch Otolaryngol Head Neck Surg.* 2002;128:751-758.
- Robbins TK et al. Consensus statement on the classification and terminology of neck dissection. *Arch Otolaryngol Head Neck Surg.* 2008;134:536-538.
- Robbins T, Medina JE, Wolfe GT, Levine PA, Sessions RB, Pruet CW. Standardizing neck dissection terminology: official report of the academy's committee for head and neck surgery and oncology. *Arch Otolaryngol Head Neck Surg.* 1991;117:601-605.
- Yamashita H, Noguchi S, Murakami N et al. Extracapsular invasion of lymph node metastasis is an indicator of distant metastasis and poor prognosis in patients with thyroid papillary carcinoma. *Cancer.* 1997;80:2268-72.
- From: Cummings, CW. *Cummings: Otolaryngology: Head and Neck Surgery.* 4<sup>th</sup> ed. Philadelphia; Mosby, Inc: 2005. (Electronic Textbook)
- Kondo T, Ezzat S, Asa SL. Pathogenetic mechanisms in thyroid follicular-cell neoplasia. *Nat Rev Cancer.* 2006;6:292- 306.
- Cheung CC, Carydis B, Ezzat S, Bedard YC, Asa SL. Molecular genetic analysis refines the fine needle aspiration diagnosis of thyroid cancer. *J Clin Endocrinol Metab.* 2001;86:2187-2190.
- Sapiro MR, Posca D, Raggioli A, et al. Detection of RET/PTC, TRK and BRAF mutations in preoperative diagnosis of thyroid nodules with indeterminate cytological findings. *Clin Endocrinol.* 2007;66:678-683.
- Kim SK, Kim DL, Han HS, et al. Pyrosequencing analysis for detection of BRAFV600E mutation in an FNAB specimen of thyroid nodules. *Diagn Mol Pathol.* 2008;17:118-125.
- Marchetti I, Lessi F, Mazzanti CM, et al. A morpho-molecular diagnosis of papillary thyroid carcinoma: BRAF V600E detection as an important tool in preoperative evaluation of fine-needle aspirates. *Thyroid.* 2009;19:837-842.
- Nikiforov YE, Steward DL, Robinson-Smith TM, et al. Molecular testing for mutations in improving fine-needle aspiration diagnosis of thyroid nodules. *J Clin Endocrinol Metab.* 2009;94:2092-2098.
- Altanerova V. Cancers connected with mutations in RET proto-oncogene. *Neoplasma.* 2001;48:325-31.
- Stoler MH. Prophylactic surgical pathology. *Am J Surg Pathol.* 2002;26:257-259.
- American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Pacini F, Schlumberger M, Sherman SI, Steward DL, Tuttle RM. Revised American Thyroid Association management

- guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid. 2009 Nov;19(11):1167-214*
- Kloos RT, Eng C, Evans DB, Francis GL, Gagel RF, Gharib H, Moley JF, Pacini F, Ringel MD, Schlumberger M, Wells SA Jr. *Medullary thyroid cancer: management guidelines of the American Thyroid Association. Thyroid. 2009 Jun;19(6):565-612.*
  - Hegedüs L, Bonnema SJ, Bennedbaek FN. *Management of simple nodular goiter: current status and future perspectives. Endocr Rev. 2003 Feb;24(1):102-32*
  - Boelaert K, Horacek J, Holder RL, Watkinson JC, Sheppard MC, Franklyn JA. *Serum thyrotropin concentration as a novel predictor of malignancy in thyroid nodules investigated by fine-needle aspiration. J Clin Endocrinol Metab. 2006 Nov;91(11):4295-301.*
  - Frates MC, Benson CB, Charboneau JW, Cibas ES, Clark OH, Coleman BG, Cronan JJ, Doubilet PM, Evans DB, Goellner JR, Hay ID, Hertzberg BS, Intenzo CM, Jeffrey RB, Langer JE, Larsen PR, Mandel SJ, Middleton WD, Reading CC, Sherman SI, Tessler FN; Society of Radiologists in Ultrasound. *Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound consensus conference statement. Radiology. 2005 Dec;237(3):794-800.*
  - Baloch ZW, LiVolsi VA, Asa SL, Rosai J, Merino MJ, Randolph G, Vielh P, DeMay RM, Sidawy MK, Frable WJ. *Diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions: a synopsis of the National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference. Diagn Cytopathol. 2008 Jun;36(6):425-37.*
  - Mehta RS, Carty SE, Ohori NP, Hodak SP, Coyne C, Lebeau SO, Tublin ME, Stang MT, Johnson JT, McCoy KL, Nikiforova MN, Nikiforov YE, Yip L. *Nodule size is an independent predictor of malignancy in mutation-negative nodules with follicular lesion of undetermined significance cytology. Surgery. 2013 Oct;154(4):730-8.*
  - Edge SB, Byrd DR, Compton CC, et al, eds. *AJCC Cancer Staging Manual, 7th ed. New York, NY: Springer; 2010.*
  - Tuttle RM, Ball DW, Byrd D, Dilawari RA, Doherty GM, Duh QY, Ehya H, Farrar WB, Haddad RI, Kandeel F, Kloos RT, Kopp P, Lamonica DM, Loree TR, Lydiatt WM, McCaffrey JC, Olson JA Jr, Parks L, Ridge JA, Shah JP, Sherman SI, Sturgeon C, Waguespack SG, Wang TN, Wirth LJ; National Comprehensive Cancer Network. *Thyroid carcinoma. J Natl Compr Canc Netw. 2010; 8: 1228-74.*
  - Hiroshi Takami, Yasuhiro Ito, et al. *Treatment of thyroid tumor : Japanese clinical guidelines. New York : Springer, 2013.*

- Cooper DS, Doherty GM, Haugen BR, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2006;16:109–142.
- Ron E, Lubin JH, Shore RE, et al. Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. *Radiat Res* 1995;141:259–277.
- Mazzaferri EL, Jhiang SM. Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. *Am J Med* 1994;97:418–428.
- Ito Y, Tomoda C, Urano T, et al. Papillary microcarcinoma of the thyroid: how should it be treated? *World J Surg* 2004;28:1115–1121.
- Sherman SI. Thyroid carcinoma. *Lancet* 2003;361:501–511.
- Ito Y, Urano T, Nakano K, et al. An observation trial without surgical treatment in patients with papillary microcarcinoma of the thyroid. *Thyroid* 2003;13:381–387.
- Henry JF, Denizot A, Puccini M, et al. [Early diagnosis of sporadic medullary cancers of the thyroid: value of systematic assay of calcitonin]. *Presse Med* 1996;25:1583–1588 [in French].
- Cooper DS, Doherty GM, Haugen BR, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2009;19:1167–1214.
- Cheung K, Roman SA, Wang TS, et al. Calcitonin measurement in the evaluation of thyroid nodules in the United States: a cost-effectiveness and decision analysis. *J Clin Endocrinol Metab* 2008;93:2173–2180.
- Newman KD, Black T, Heller G, et al. Differentiated thyroid cancer: determinants of disease progression in patients <21 years of age at diagnosis: a report from the Surgical Discipline Committee of the Children's Cancer Group. *Ann Surg* 1998;227:533–541.
- Robie DK, Dinauer CW, Tuttle RM, et al. The impact of initial surgical management on outcome in young patients with differentiated thyroid cancer. *J Pediatr Surg* 1998;33:1134–1138; discussion 1139–1140. Sherman SI, Brierley JD, Sperling M, et al. Prospective multicenter study of thyroid carcinoma treatment: initial analysis of staging and outcome. National Thyroid Cancer Treatment Cooperative Study Registry Group. *Cancer* 1998;83:1012–1021.
- Tsang RW, Brierley JD, Simpson WJ, et al. The effects of surgery, radioiodine, and external radiation therapy on the clinical outcome of patients with differentiated thyroid carcinoma. *Cancer* 1998;82:375–388. Dottorini ME, Vignati A, Mazzucchelli L, et al. Differentiated thyroid carcinoma in children and adolescents: a 37-year experience in 85 patients. *J Nucl Med* 1997;38:669–675.

- Samuel AM, Rajashekharao B, Shah DH. Pulmonary metastases in children and adolescents with well-differentiated thyroid cancer. *J Nucl Med* 1998;39:1531–1536.
- Hay ID, Bergstrahl EJ, Goellner JR, et al. Predicting outcome in papillary thyroid carcinoma: development of a reliable prognostic scoring system in a cohort of 1779 patients surgically treated at one institution during 1940 through 1989. *Surgery* 1993;114:1050– 1057; discussion 1057–1058.
- Shaha AR, Loree TR, Shah JP. Prognostic factors and risk group analysis in follicular carcinoma of the thyroid. *Surgery*  
1995;118:1131–1136; discussion 1136–1138.
- DeGroot LJ, Kaplan EL, Straus FH, Shukla MS. Does the method of management of papillary thyroid carcinoma make a difference in outcome? *World J Surg* 1994;18:123–130.
- Miccoli P, Antonelli A, Spinelli C, et al. Completion total thyroidectomy in children with thyroid cancer secondary to the Chernobyl accident. *Arch Surg* 1998;133:89–93.
- Palme CE, Waseem Z, Raza SN, et al. Management and outcome of recurrent well-differentiated thyroid carcinoma. *Arch Otolaryngol Head Neck Surg* 2004;130:819–824.
- Frankenthaler RA, Sellin RV, Cangir A, Goepfert H. Lymph node metastasis from papillary-follicular thyroid carcinoma in young patients. *Am J Surg* 1990;160:341–343. 65. LiVolsi VA. Follicular lesions of the thyroid. In: LiVolsi VA, ed. *Surgical Pathology of the Thyroid*. Philadelphia, PA: WB Saunders; 1990:173–212.
- Brennan MD, Bergstrahl EJ, van Heerden JA, McConahey WM. Follicular thyroid cancer treated at the Mayo Clinic, 1946 through 1970: initial manifestations, pathologic findings, therapy, and outcome. *Mayo Clin Proc* 1991;66:11–22.
- Belchetz G, Cheung CC, Freeman J, et al. Hurthle cell tumors: using molecular techniques to define a novel classification system. *Arch Otolaryngol Head Neck Surg* 2002;128:237–240.
- Chen H, Nicol TL, Zeiger MA, et al. Hurthle cell neoplasms of the thyroid: are there factors predictive of malignancy? *Ann Surg* 1998;227:542–546.
- Thompson NW, Dunn EL, Batsakis JG, Nishiyama RH. Hurthle cell lesions of the thyroid gland. *Surg Gynecol Obstet* 1974;139:555–560.
- Lopez-Penabad L, Chiu AC, Hoff AO, et al. Prognostic factors in patients with Hurthle cell neoplasms of the thyroid. *Cancer* 2003;97:1186–1194.

- Khafif A, Khafif RA, Attie JN. Hurthle cell carcinoma: a malignancy of low-grade potential. *Head Neck* 1999;21:506–511.
- Samaan NA, Schultz PN, Hickey RC, et al. The results of various modalities of treatment of well differentiated thyroid carcinomas: a retrospective review of 1599 patients. *J Clin Endocrinol Metab* 1992;75:714–720.
- Samaan NA, Schultz PN, Haynie TP, Ordonez NG. Pulmonary metastasis of differentiated thyroid carcinoma: treatment results in 101 patients. *J Clin Endocrinol Metab* 1985;60:376–380.
- Sugino K, Ito K Jr, Ozaki O, et al. Papillary microcarcinoma of the thyroid. *J Endocrinol Invest* 1998;21:445–448.
- Hay ID. Papillary thyroid carcinoma. *Endocrinol Metab Clin North Am* 1990;19:545–576.
- Emerick GT, Duh QY, Siperstein AE, et al. Diagnosis, treatment, and outcome of follicular thyroid carcinoma. *Cancer* 1993;72:3287–3295.
- Yamashita H, Noguchi S, Murakami N, et al. Extracapsular invasion of lymph node metastasis is an indicator of distant metastasis and poor prognosis in patients with thyroid papillary carcinoma. *Cancer* 1997;80:2268–2272.
- Sellers M, Beenken S, Blankenship A, et al. Prognostic significance of cervical lymph node metastases in differentiated thyroid cancer. *Am J Surg* 1992;164:578–581.
- Lindegaard MW, Paus E, Hoie J, et al. Thyroglobulin radioimmunoassay and  $^{131}\text{I}$  scintigraphy in patients with differentiated thyroid carcinoma. *Acta Chir Scand* 1988;154:141–145.
- Schlumberger M, Challeton C, De Vathaire F, Parmentier C. Treatment of distant metastases of differentiated thyroid carcinoma. *J Endocrinol Invest* 1995;18:170–172.
- Sisson JC, Giordano TJ, Jamadar DA, et al.  $^{131}\text{I}$  treatment of micronodular pulmonary metastases from papillary thyroid carcinoma. *Cancer* 1996;78:2184–2192.
- Brown AP, Greening WP, McCready VR, et al. Radioiodine treatment of metastatic thyroid carcinoma: the Royal Marsden Hospital experience. *Br J Radiol* 1984;57:323–327.
- Casara D, Rubello D, Saladini G, et al. Different features of pulmonary metastases in differentiated thyroid cancer: natural history and multivariate statistical analysis of prognostic variables. *J Nucl Med* 1993;34:1626–1631.
- Lin JD, Kao PF, Weng HF, et al. Relative value of thallium-201 and iodine-131 scans in the detection of recurrence or distant metastasis of well differentiated thyroid carcinoma. *Eur J Nucl Med* 1998;25:695–700.

- Hay ID, Grant CS, Taylor WF, McConahey WM. Ipsilateral lobectomy versus bilateral lobar resection in papillary thyroid carcinoma: a retrospective analysis of surgical outcome using a novel prognostic scoring system. *Surgery* 1987;102:1088–1095.
- Hay ID, Grant CS, Bergstrahl EJ, et al. Unilateral total lobectomy: is it sufficient surgical treatment for patients with AMES low-risk papillary thyroid carcinoma? *Surgery* 1998;124:958–964.
- Dackiw AP, Zeiger M. Extent of surgery for differentiated thyroid cancer. *Surg Clin North Am* 2004;84:817–832.
- Shaha AR. Implications of prognostic factors and risk groups in the management of differentiated thyroid cancer. *Laryngoscope* 2004;114:393–402.
- DeGroot LJ, Kaplan EL. Second operations for “completion” of thyroidectomy in treatment of differentiated thyroid cancer. *Surgery* 1991;110:936–939; discussion 939–940.
- Scheumann GF, Seeliger H, Musholt TJ, et al. Completion thyroidectomy in 131 patients with differentiated thyroid carcinoma. *Eur J Surg* 1996;162:677–684.
- Chao TC, Jeng LB, Lin JD, Chen MF. Completion thyroidectomy for differentiated thyroid carcinoma. *Otolaryngol Head Neck Surg* 1998;118:896–899.
- Pacini F, Elisei R, Capezzzone M, et al. Contralateral papillary thyroid cancer is frequent at completion thyroidectomy with no difference in low- and high-risk patients. *Thyroid* 2001;11:877–881.
- Burge MR, Zeise TM, Johnsen MW, et al. Risks of complication following thyroidectomy. *J Gen Intern Med* 1998;13:24–31.
- Udelsman R, Lakatos E, Ladenson P. Optimal surgery for papillary thyroid carcinoma. *World J Surg* 1996;20:88–93.
- Pattou F, Combemale F, Fabre S, et al. Hypocalcemia following thyroid surgery: incidence and prediction of outcome. *World J Surg* 1998;22:718–724.
- Mazzaferri EL, Kloos RT. Clinical review 128: current approaches to primary therapy for papillary and follicular thyroid cancer. *J Clin Endocrinol Metab* 2001;86:1447–1463.
- Mazzaferri EL. Thyroid remnant 131I ablation for papillary and follicular thyroid carcinoma. *Thyroid* 1997;7:265–271.
- Taylor T, Specker B, Robbins J, et al. Outcome after treatment of high-risk papillary and non-Hurthle-cell follicular thyroid carcinoma. *Ann Intern Med* 1998;129:622–627.

- Leger FA, Izembart M, Dagousset F, et al. Decreased uptake of therapeutic doses of iodine-131 after 185-MBq iodine-131 diagnostic imaging for thyroid remnants in differentiated thyroid carcinoma. *Eur J Nucl Med* 1998;25:242–246.
- Muratet JP, Giraud P, Daver A, et al. Predicting the efficacy of first iodine-131 treatment in differentiated thyroid carcinoma. *J Nucl Med* 1997;38:1362–1368.
- Mazzaferri EL. Carcinoma of follicular epithelium: Radioiodine and other treatment outcomes. In: Braverman LE, Utiger RD, eds. *The Thyroid: A Fundamental and Clinical Text*. Philadelphia, PA: Lippincott-Raven; 1996:922–945.
- Brierley J, Maxon HR. Radioiodine and external radiation therapy in the treatment of thyroid cancer. In: Fagin JA, ed. *Thyroid Cancer*. Boston, MA: Kluwer Academic; 1998:285–317.
- Tuttle RM, Leboeuf R, Robbins RJ, et al. Empiric radioactive iodine dosing regimens frequently exceed maximum tolerated activity levels in elderly patients with thyroid cancer. *J Nucl Med* 2006;47:1587–1591.
- Van Nostrand D, Wartofsky L. Radioiodine in the treatment of thyroid cancer. *Endocrinol Metab Clin North Am* 2007;36:807–822, vii–viii.
- Maxon HR III, Englano EE, Thomas SR, et al. Radioiodine-131 therapy for well-differentiated thyroid cancer—a quantitative radiation dosimetric approach: outcome and validation in 85 patients. *J Nucl Med* 1992;33:1132–1136.
- Benua RS, Cicale NR, Sonenberg M, Rawson RW. The relation of radioiodine dosimetry to results and complications in the treatment of metastatic thyroid cancer. *Am J Roentgenol Radium Ther Nucl Med* 1962;87:171–182.
- Sherman SI, Tielens ET, Sostre S, et al. Clinical utility of posttreatment radioiodine scans in the management of patients with thyroid carcinoma. *J Clin Endocrinol Metab* 1994;78:629–634.
- Pacini F, Molinaro E, Castagna MG, et al. Recombinant human thyrotropin-stimulated serum thyroglobulin combined with neck ultrasonography has the highest sensitivity in monitoring differentiated thyroid carcinoma. *J Clin Endocrinol Metab* 2003;88:3668–3673.
- Haugen BR, Pacini F, Reiners C, et al. A comparison of recombinant human thyrotropin and thyroid hormone withdrawal for the detection of thyroid remnant or cancer. *J Clin Endocrinol Metab* 1999;84:3877–3885.
- Kloos RT, Mazzaferri EL. A single recombinant human thyrotropin-stimulated serum thyroglobulin measurement predicts differentiated thyroid carcinoma metastases three to five years later. *J Clin Endocrinol Metab* 2005;90:5047–5057.
- Ladenson PW, Braverman LE, Mazzaferri EL, et al. Comparison of administration of recombinant human thyrotropin with withdrawal of thyroid hormone for radioactive iodine scanning in patients with thyroid carcinoma. *N Engl J Med* 1997;337:888–896.