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內文：

Introduction

1. 這篇文章主要討論為下列惡性腫瘤治療所實行的neck dissections(NDs)
 - (1) Oral SCC
 - (2) Pharyngeal and laryngeal SCC
 - (3) Salivary gland malignancies
2. 根據治療的indications，NDs可分為
 - (1) therapeutic
 - (2) elective

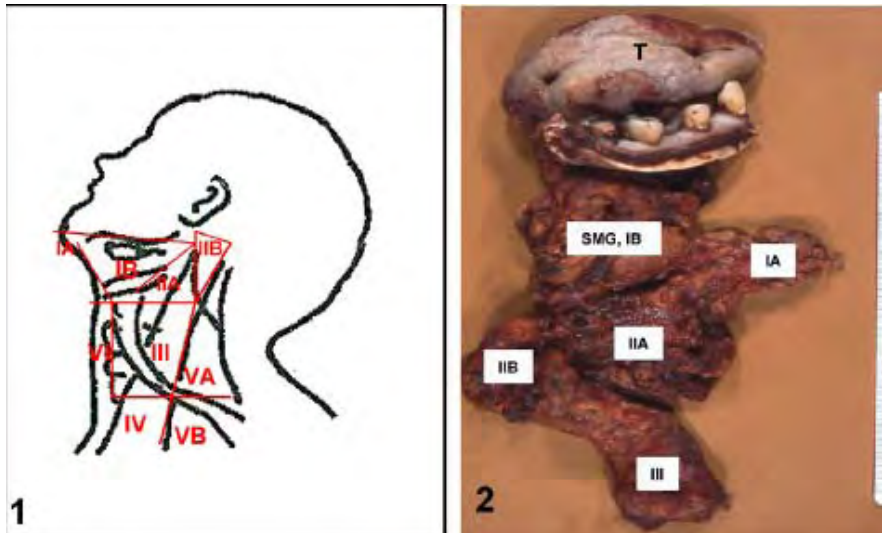
兩者依據是否有clinical/radiological suggestion of metastasis來區分。Salvage NDs則用於late presenting or recurrent disease
3. Relation to the timing of primary tumor resection
 - (1) May be simultaneously with primary tumor resection. (也可能不同時間進行)
 - (2) Simultaneous ND may or may not be in continuity with primary resection
4. Relation to the site of primary tumor
 - (1) Unilateral – 同側(ipsilateral)或異側(contralateral)
 - (2) Bilateral
5. Classifications
 - (1) Radical (Classical) ND -- en bloc removing
 - a. Level I-V lymph nodes
 - b. Internal jugular vein (IJV)
 - c. SCM muscle
 - d. Spinal accessory nerve
 - (2) Extended RNDs – 包含額外的組織結構，例如: skin
 - (3) Functional preserving NDs – 不包含IJV與SCM muscle，依所移除lymph nodes分佈的範圍可分為：
 - a. Comprehensive (又稱modified RND、Bocca procedure) – 包含level I-V
 - b. Selective – 移除有highest risk of metastasis的nodal levels，
 - Oral cavity cancer – level I-III，最下緣到junction between the superior belly of the omohyoid muscle and the IJV。
 - Oral tongue cancer – level I-IV，又稱extended supraomohyoid NDs 或anterolateral NDs。

Topography, terminology and some theoretical considerations of cervical lymph node metastases

1. Robins et al – six main cervical anatomic levels

Table 1 Cervical lymph nodes—anatomical levels and nodal characteristics.

Anatomical level	Boundaries	Usual no. of nodes	Nodal characteristics	Principal drainage basin
Sublevel IA, submental	Within the submental triangle between the anterior bellies of the digastric muscles and the hyoid bone.	3–4	Spherical, <10 mm	Lower lip, anterior lower alveolar ridge, anterior floor of mouth, tip of tongue.
Sublevel IB, submandibular	Within the boundaries of the anterior belly of digastric, stylohyoid and body of mandible, close to the submandibular salivary gland and facial artery.	3–7	Round, flattened, <18 mm	Submental and facial nodes. Labial and buccal mucosae, palate, oral tongue, floor of mouth.
Level II, upper jugular; level IIA; level IIB	Located around the upper 1/3 of the internal jugular vein and adjacent spinal accessory nerve extending from the level of the skull base to the inferior border of the hyoid bone, and from the stylohyoid muscle to the posterior border of the sternocleidomastoid muscle. Anterior to the spinal accessory nerve. Posterior to the spinal accessory nerve.	10–20	Bean-shaped, <25 mm ill-defined, flat, round or bean-shaped, 3–20 mm	Submental, submandibular, occipital, posterior auricular, parotid and retropharyngeal nodes. Oral and nasal cavities, pharynx, larynx, parotid gland.
Level III, middle jugular	Around the middle 1/3 of the internal jugular vein, at the level of the bifurcation of the common carotid artery, extending from the inferior border of the hyoid bone to the inferior border of the cricoid cartilage.	5–10	Long, slender, flat, <20 mm	Upper jugular nodes. Mid-portion of oral tongue.
Level IV, lower jugular	Around the lower 1/3 of the internal jugular vein where the anterior belly of omohyoid crosses the internal jugular vein, extending from the inferior border of the cricoid cartilage to the clavicle.	5–10	Bean-shaped and spherical, <25 mm	Upper and middle jugular nodes. Tip of tongue, anterior floor of mouth, hypopharynx, thyroid, cervical oesophagus and larynx.
Level V, posterior triangle; sublevel VA; sublevel VB	Extends from the apex formed by the convergence of the sternocleidomastoid and trapezius muscles, the clavicle, posterior border of sternocleidomastoid and anterior border of trapezius. Spinal accessory nodes, above inferior border of cricoid notch. Transverse cervical and supraclavicular nodes.	20–30	Flat, round and bean-shaped, <15 mm	Occipital and posterior auricular nodes. Naso and oropharynx, skin of scalp and neck.
Level VI; anterior compartment	Pretracheal and paratracheal, precricoid and perithyroidal nodes. Extends from hyoid bone, sternal notch, common carotid artery.	10–20	Small, ovoid, <10 mm	Thyroid gland, glottic and subglottic larynx, apex of pyriform sinus, cervical oesophagus.



2. Lymph node metastasis in SCC and salivary gland malignancies
 -- embolic spread, entering the lymph nodes
 (1) via afferent lymphatics and traversing the capsule
 (2) around valves, as a capsular(juxtacapsular) embolus (Fig. 3)

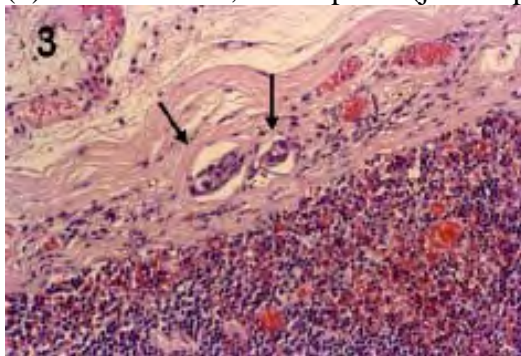
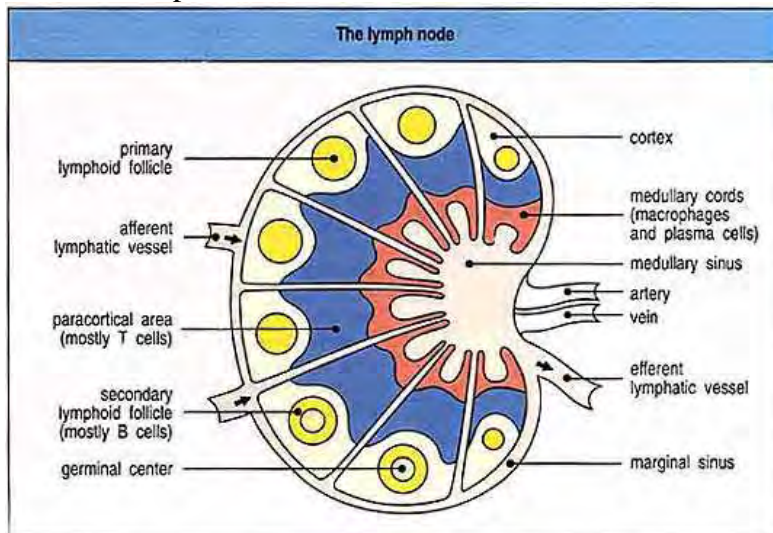


Fig.3
 Lymphatic embolism in a cervical lymph node. Groups of coherent carcinoma cells (arrows) have been transported in the lymph stream to the capsule of the node.

- (3) via the marginal, cortical and medullary sinuses
 The embolus must settle and establish a vascular stroma in order to develop into a metastatic deposit.



3. Development of lymph node metastasis
 (1) Emboic
 a. Size : not more than 0.2mm in greatest dimension
 b. Definition : isolated tumour cells (ITC)

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- (2) Tumour deposits
 - a. 0.2 and 2mm → micrometastases
successful settling and growth (mitotic activity, stromal reaction)
 - b. > 2mm → conventional metastasis
Covert metastasis -- not suspected clinically or radiologically; may be ITC, micrometastases or conventional metastases
 - (3) Once established within the lymph node, the tumor deposit(s) grow(s) at variable rate to replace the lymphoid parenchyma
 4. Drainage route of metastasis
 - (1) Initially, metastasis develops in one or more lymph nodes directly draining the lymphatic basin of the primary tumor
 - (2) Then they progresses in an orderly “overflow” fashion to produce an “inverted-cone” shape where the disease is maximal within the first echelon of nodes with a gradual spread to successive levels
 - (3) Simultaneous involvement of multiple drainage routes
 - oral tongue tumours(30%)、floor-of-mouth tumours (20%)、oropharyngeal tumours (10%)
 - 形成
 - a. “Skip” metastases
Metastasis in a node at level I and a node at level IV without evidence of metastasis at levels II and III
 - b. “Peppering” of nodes at multiple anatomical levels
denotes micrometastasis in multiple nodes in the absence of a conventional metastasis
 - (4) Extracapsular (extranodal) spread (ECS)
SCC with metastasis -- Often , oropharyngeal tumors with metastasis-- 70% cases
 - (5) Simultaneous bilateral metastases -- 15–20% of floor-of-mouth, oral tongue and pharyngeal tumours with metastasis
 5. 除上述六種cervical lymph node level 外，下列其它的lymph node groups在salivary gland malignancies也可能會被侵犯，SCC則較少
 - (1). The parotid lymph nodes
 - usually be removed by total or partial parotidectomy often in continuity with the ND.
 - a. Number : mean 20 (range 10–35)
 - b. Shape : round or bean-shaped
 - c. Size : 10mm
 - d. subdivided into extraglandular (pre-auricular and infra-auricular) and intraglandular groups.
 - (2). Facial nodes (mandibular, buccal, infra-orbital and malar)
 - a. Shape : bean-shaped
 - b. Size : 10mm
 - c. Involved tumor -- retromolar tumors with metastases →15%
alveolar and buccal tumors → less frequently
 - (3) Sublingual and lingual nodes
 - a. Inconstant small nodes (up to 4) associated with the sublingual glands and midline lingual raphe
 - b. Very occasionally involved in oral tongue and floor-of-mouth tumors
 - (4) Retropharyngeal nodes
-

occasionally involved by nasopharyngeal and oropharyngeal tumours

Specimen presentation

1. Orientation

In order for the pathologist to visualise the cervical lymph nodes in their correct anatomical relationships, the surgical team must pin out the ND specimen prior to fixation

-- 將specimen釘在或縫在cork / polystyrene tile板上，外側朝上

2. Labeling

Function-preserving dissections 缺乏 landmarks，所以要用suture或tag放在中間來標誌each anatomical nodal level. A simple line diagram or labelled photograph should be submitted with the Pathology Request Form if the request form does not include a pre-printed diagram

4. Fixation

放入 a container full of a formaldehyde-based solution for 24–48 h 下列要點須提醒外科人員注意

- (1) not allowing the specimen to dry out prior to fixation
- (2) not to use overtight sutures that may lead to tearing of the specimen and delay fixation of the deep aspect of the dissection

5. Alternative method of specimen presentation

- (1) Divided the Nd into its component anatomical levels and then place each nodal level in a separate container. A suture can be used to indicate the orientation of the tissue
- (2) ND in continuity with resection of primary tumor -- caution should be used as attempts to divide levels I and II nodes may disrupt the integrity of the primary tumor resection

Macroscopic assessment, harvesting and trimming of lymph nodes

1. Macroscopic assessment

- (1) Beginning with a description of the type of ON
- (2) Following a system— orientate the specimen then begin with the outer aspect and then the deep aspect
- (3) A standard radical ND
 - a. outer aspect –
 - the submandibular salivary gland at the anterosuperior corner
 - the broad SCM crossing diagonally
 - the omohyoid muscle protruding from the lower end of the SCM
 - the external jugular vein and the spinal accessory nerve crossing the SCM
 - the tail of the parotid gland around the superior cut end of the SCM
 - additional structures may be included such as skin or the stylohyoid and digastric muscles, or the complete parotid gland
 - b. deep aspect -- the IJV running from superior to inferior
- (4) If enlarged nodes or tumour are visible on the surface of the specimen, the area should be inked to facilitate assessment of the surgical boundaries

2. Identification of lymph node – inspection and palpation with gloved fingers

- (1) Increasing the fixation time beyond 24 h makes nodes more palpable
- (2) Smaller nodes, particularly those in level V may resemble adipose tissue in color → to process any uncertain material since histology often reveals small nodes within adipose tissue
- (3) Knotted suture material (for example, tying off vessels) may simulate a nodule → close inspection 即可分辨

3. Harvesting and trimming -- 第一種方法

Level I first, then level II → they both easily separated off from the SCM, 可個別處理

Then level IV, III, II, from deep aspect to the limits of the three jugular levels

- (1) Discrete node – 一顆顆 dissected out with attached pericapsular adipose tissue
- (2) Larger nodes (around 10mm or more) -- 應剖半或平行長軸經 hilum 處切片
- (3) 明顯的 metastatic tumor -- 測量大小並剖半或切片 (slice), 具有較多 metastatic deposits 的那一半或切片應與 perinodal tissues (the IJV, SCM, submandibular salivary gland as appropriate) 一起被 processed, 可顯示 the extent of extracapsular spread
- (4) Matted nodes -- 測量大小, 計算其構成這個 mass 的 lymph node 數量, 切片 (slicing) 後連同周遭 tissue 放入 block 後 process, 可顯示其 peripheral extent
- (5) Nodes/nodal masses with cystic lumen – 測量後剖半或切片 (slice)
 - a. 適當的量出包含 cystic lumen 的最大直徑
 - b. 所選擇的 tissue block 要能表現出 the cyst wall/peripheral extent of the tumour
- (6) Node fixed to the IJV—slices showing the relation should be included the adherence may be due to fibrosis rather than tumour
- (7) Any areas with suspected ulceration of the intima/thrombosis should be processed.
- (8) Node appearing negative – both halves should be processed. Re-slicing the bisected node at 90 degree to create multiple hemispherical sections permits the assessment of greater areas of the subcapsular sinuses
- (9) Small or flat nodes should be processed whole, and several nodes (from the same anatomical level) can be processed in the same cassette
- (10) Labelling cassettes
 - To develop a system
 - e.g. : a. different identifying letters for each anatomical level
A – level I, B – level II, etc.
 - b. followed by a number for each cassette containing a node or collection of small nodes (A1, A2, etc.)
 - To keep a note of whether the node has been bisected or sliced, especially if several cassettes are needed for the same node
 - Added care at this stage facilitates later stages of the assessment and report writing

4. Selective NDs.—similar method described above

These are often easier to deal with since the lymph nodes are not obscured by other anatomical structures and the extent of metastasis is usually minimal

5. Salvage NDs -- can be difficult to orientate and are often distorted by fibrosis

Tumour may not be macroscopically distinguishable from scar tissue

-- >embed multiple slices of any doubtful tissue

6. Macroscopic documentation 應包含

- for each level –
- (1) the number of harvested nodes
 - (2) the diameter of the largest node
 - (3) the macroscopic suspicion of tumour
 - (4) extracapsular spread

7. Harvesting and trimming –其它方法

- (1) 將每個 anatomical level 的 content 切成 into 2–3mm thick blocks, 其中的

lymph nodes都留在原位

- a. This produces a good nodal yield and good detection of small tumour deposits
- b. Caution and concentration are essential in order to “reconstruct” nodes appearing in multiple blocks and hence, avoid exaggerating the number of nodes and the number of metastases

(2) Clearing techniques

利用 solvents使 adipose tissue 變透明，可使lymph nodes的 detection 與 harvest 變更容易，但要花很多時間

8. Numbers of lymph nodes .yielding

- (1) RND --around 40 lymph nodes
- (2) Levels I–IV dissection -- around 30 nodes

The precise number varies depending on the patient’s age, the extent of metastasis, previous radiotherapy, and so on

Histological assessment

在 routine diagnostic service中，完整的assessment與可獲得的資源之間應取得平衡，因此下列妥協是被廣泛接受的 → to assess a single HE-stained section from each tissue block and to use step-serial sections and/or immunohistochemistry (IHC) in selected cases.

1. Selected cases

- (1) To distinguish between a micrometastasis and a conventional metastasis
- (2) To assess the extent of extracapsular spread
- (3) To confirm the epithelial nature of a suspicious area

2. Microscopic assessment

- (1) Each slide should be scanned at low power paying particular attention to the nodal sinuses. Suspected tumor deposits should be examined at higher magnification to confirm their epithelial nature
- (2) 關於 tumor deposits 的下列資訊應記錄下來
 - a. Site – subcapsular or central
 - b. Solid or cystic
 - c. Profile parameter – 會影響micrometastases 的診斷與conventional metastasis的pN category
- (3). 若一個positive的node中有 multiple tumor islands，則這些islands個別的 diameter應被測量相加，而非將整個nodal parenchyma都包含進去 → 現實中有困難，當tumor island太小或為single cell時，此時可測量被tumor 影響到的區域的 diameter。
- (4) It may be necessary to use the macroscopic dimension in nodes showing expansion and cystic change.

The assessment of extracapsular spread (ECS)

1. ECS為post-operative radiotherapy 的criterion，也是important predictor of regional relapse與SCC-related death，因此準確的偵測 ECS 很重要。ECS可能發生在 small lymph nodes，或 tumour deposits < 2mm 的 lymph nodes(the tumor deposits located in capsular or subcapsularsinuses or peripheral cortex)。Extensive ECS 在巨觀下就很明顯，但仍需 histological 確認

2. Recording ECS –

- (1)第一種方式 -- reference to the tissues and structures involved:
 - a. Perinodal adipose tissue.
 - b. Blood vessels such as the facial vessels and the IJV and carotid artery—this

- may be confined to the outer sheath or involve the various layers of the vessel wall, or there may be full thickness involvement with intima ulceration and thrombosis
- c. The fascia of striated muscle or the muscle itself, most commonly the digastric and SCM
 - d. Salivary gland parenchyma. For example, involvement of the submandibular gland is a particularly poor prognostic feature
 - e. The mandible—either the periosteum or the bone
- (2) 另一種方式
estimating the distance (in mm) from a reconstruction of the original position of the node capsule
- (3) 下列項目也應被記錄
- a. Number of nodes at each anatomical level showing ECS
 - b. the greatest extent at each level
3. 在 lymph drainage area 的 connective tissue 中可能會出現明顯的 tumor nodule，而且沒有可辨識為 residual lymph node structure 的 histological evidence，The UICC 建議
- (1) 將之視為 nodal metastasis，若這個 tumor nodule 仍有 lymph node 的樣子與平滑的外形。
- (2) 將之視為 venous invasion (V category) 或 discontinuous extension of the primary tumour (T category)，若其外形為不規則形狀。
- 兩者的區別將影響 staging (後者可能歸類為 pN0)。
- eg: primary tumour – floor of mouth
tumour nodule – one single nodule deep to the primary tumor
smooth → metastasis to a sublingual node, pN1
irregular → venous invasion or discontinuous extension of the primary tumor, pN0
4. multiple tumor nodules with obvious nodal metastases and ECS 比較常見，這種情形下，因為 matting 所以無法準確算出 positive lymph node 的數量，只能估計大概數量 (前面要加上 at least)。
5. Early ECS 或 microscopic ECS
- (1) often challenging
 - (2) Peripherally located or subcapsular tumour may abut onto the node capsule and may be accompanied by stromal reaction (desmoplasia)
 - (3) When a single node is suspicious for ECS and there is no obvious ECS elsewhere in the ND, additional step-serial sections should be examined
- 若 step-serial sections，無 ECS 發現，則將之視為局限於 lymph node 內的 metastasis 應是安全的。
- 若 lymph node 有 bulging (hump, hillock)，則應記錄為 ECS confined to the pericapsular tissues。
- 沒有特殊染色可區分這兩種情形，而在 capsular sinuses 或 the perinodal lymphatic vessels 中發現 emboli of tumor or ITC 並不構成 ECS，but they should be noted since they appear to have additional prognostic value
6. Marking the slide label with the tumor dimension and an arrow to indicate ECS on each slide at the time of the histological assessment expedites Sentinel node biopsy
1. 對 ipsilateral and contralateral N0 necks，可以 lymphoscintigraphy 與在 tumor

bed注射藍色染劑來偵測lymph node, 但成功與否取決在primary tumor的大小、位置與操作者的技術, 目前對sentinel nodes應如何檢查並沒有共識。

2. Fresh lymph nodes 的frozen sections可能會危害到之後對paraffin-embedded tissue完整詳細的評估
3. 將complete serial sectioning of the paraffin block當做固定程序是不實際的, 妥協的作法為以150mm 為間距的step-serial sectioning, 並且以HE及AE1/AE3免疫化學染色來檢查。

Potential pitfalls

1. 數種lymph nodes的reactive changes 可能會造成混淆, 誤認為轉移
 - (1) sinus histiocytosis
 - (2) vascular transformation of sinuses
 - (3) changes in germinal centres
 - (4) hyaline change within lymphoid parenchyma
 - (5) Granulomatous reaction in lymph nodes, 然而對small metastatic deposits與keratin deposition的foreign-body granuloma也可能會發生. 同時有granulomatous disease, 例如: tuberculosis, 的可能性也應考慮
2. 數種良性的cellular inclusions可能會出現在lymph nodes內或lymph nodes旁, 應小心與轉移區分
 - (1) salivary epithelium
 - (2) thyroid epithelial inclusions, 常見在levels III 或 IV
 - (3) nevus cell rests

可用免疫組織化學染色(IHC)幫助鑑別診斷一些lesions, 約有1% 具有轉移的病人, 轉移的表皮細胞分布在多個解剖區域lymph nodes的nodal sinuses 之間, 易被誤判為sinus histiocytosis, IHC 對這種情況很有用。

3. Cystic metastases 以及它們與branchial cyst、primary branchial carcinoma 的鑑別診段常在文獻中被討論, 病人的年紀很重要, 超過40歲的病人, 應將整個“cyst”都進行處理以step/serial sections來檢查, 因為cyst lining大部份區域可能都呈現benign appearance。
4. 除了conventional SCC, 數種次分類的SCC發生轉移也在文獻中完整的描述; Hybrid tumors 也曾出現, 它們的轉移可能會引起混淆, 因為可能只表現其中一種腫瘤的轉移模式。

Report writing and presentation of findings

使用圖表總結lymph node 轉移的情形(如下圖), 並在報告中記錄TNM stage.

Level	Total	Tumour	ECS
IA			
IB			
IIA			
IIB			
III			
IV			
VA			
VB			
VI			

Total = total number of nodes examined;
 Tumour = total number of tumour involved nodes; ECS = presence of ECS; NI = not included in dissection