口腔病理科病例報告

“ Intern C: 林士軒 林士涵 周揚智 周桂蓮
指導老師：陳玉昆主任 林立民教授 暨口病科全體醫師
“ 2014/10/28 TUE.
Name: OOO
Sex: Female
Age: 65 y/o
Native: 屏東縣
Marital status: 已婚
Attending V.S.: OOO 医師
First visit: 97/11/26
A mass on L’t tongue border on 103/07/30
Location: L’t lateral tongue border

Dimension: ~2.5×2.5cm

Color: Red

Shape: Irregular

Surface: Lobulated

Mobility: Fixed

Consistency: Rubbery

Pain: ?

Induration: +

Lymphadenopathy: ?
97/11/26

"First time to OS dept.

"Incisional biopsy H-P: SCC, L’t lower post gingiva, cT2N1M0, Stage III
Present Illness

97/12/18

OP: WE + Segmental resection + SOND + reconstruction plate repair + Terudermis repair

Post op H-P:

1. SCC, grade I, T1N1M0, stage III
   Tumor size: 1.5x1.4x0.7cm
   Surgical margins: involved (36 lingual gingiva)
   Bone invasion: present

2. Lymph nodes status: metastatic squamous cell carcinoma, 1/8 over submandibular region
Present Illness

98/2/11-2/16
“Post op radiotherapy at 安泰 H 6 times

98/04/16-100/9/14
“Routine f/u

100/09/14
“Mass over anterior mandible area
“Incisional biopsy
“H-P: SCC , lower anterior gingiva, cT4aN0M0, stage IVa
Present Illness

100/10/20

OP: WE + partial mandibulectomy + reconstruction plate repair + tongue flap repair

H-P: SCC grade I, lower lip, pT4cN0cM0, stage IV

SCC grade I, mandible, invasion

Tumor size: 2.0x1.5x0.5cm

Bone invasion: present

Surgical margins: involved

Cannot close mouth after surgery, arranged PS operation
100/10/24
“OP: Sup. Vena cava catheterization via R’t cephalic vein

100/10/28 (PS dept) post-OP 1wk
“OP: Post tracheostomy + ALT free flap reconstruction

100/12/7
“Post op RT at KMU halted, transferred to OOH for further tx
101/03/07

"Complicated with chin fistula"

"Curretage H-P: necrotic tissue"
Ulcer and bone exposure on tooth 43-45 lingual gingiva

Incisional H-P:
1. mild severe epithelial hyperplasia, lower R’t gingiva
2. Sequestrum w/ bacterial colonies, tooth 43 area,
102/02/06

ORN and reconstruction plate exposure
Present Illness

102/2/26

"OP: debride + remove reconstruction plate + complicated ext 45-47

"Edentulous ridge curetage H-P:

"1. SCC, gr 1, R’t edentulous ridge lesion

"2. Pyogenic granuloma, lower L’t ridge lesion
102/03/25

C/T found Residual/recurrent tumor

102/03 - 102/05

3 courses CCRT w/ TPF

102/07/25

Discomfort over L’t mandible area

incisional H-P:

1. sequestrum, L’t Md

2. bacterial colonies, hemorrhage, lower L’t gingiva
102/09/18 ~ 10/16
CCRT cisplatin

102/11/07
Suspect ORN, R’t Md curretage H-P:
Sequestrum, necrotic tissue, R’t Md

103/02/20
OP: sequestectomy over R’t Md
H-P: sequestrum formation and fibrosis of marrow tissue, compatible with ORN, R’t Md
103/04/16

"R/O neck lymph node noted

"CT: necrotic meta lymphadenopathy in R’ t level IIA, 1.9cm

"Arrange RND 103/06/05
"Operation under GA(R’ t RND)"

"H-P report showed: Lymph node, stated as right neck lymph node, lymphadenectomy, carcinoma, metastatic(1/2) (pN1cM0,stage III)"
103/06/18-103/07/02
“Check wound, pain on occipital area

103/07/30
“A mass on L’t tongue border, surface smooth, induration(+) 3x1 cm in diameter
“In-biopsy==> H-P report*
Past Medical History

- Underlying disease: (+) GERD, gr. B
- Hospitalization (+): SCC
- Surgery under GA (+): SCC
- Drug allergy history: (-)

Past Dental History

- General routine dental treatment
- Attitude to dental treatment: co-operative
Risk factor related to malignancy

- Alcohol: (+) 3 cup/d, 30y, quit 5y
- Betel: (+) 20 grains/d, 30y, quit 5y
- Cigarette: (-)

Special oral habits: Denied
• Surgical defect: from symphysis of mandible to ascending ramus (left side)
• Missing teeth: 28, 31, 34, 35, 36, 37, 38, 41
• Reconstruction plate
• Surgical defect: from body of right mandible to ascending ramus of left mandible
• Missing teeth: 28,31,32,33,34,35,36,37,38,41,42,43,44
• Reconstruction plate
• Surgical staple
Image finding – Panorex
• Surgical defect
• Remaining teeth: 11,12,13,14,15,16,17,21,22,23,24,25,26,27,28
• Surgical staple
• Surgical defect
• Surgical staple
• Surgical defect: from ascending ramus of right mandible to ascending ramus of left mandible
• Remaining teeth: 11,12,13,14,15,16,17,21,22,23,24,25,26,27,28
• Surgical staple
Image finding – oral CT (102/03/25)
Image finding – oral CT (103/05/07)
Impression:

“An necrotic metastatic lymphadenopathy in the right level IIA. (1.9cm@Se/Im:3/25)
Image finding – CT (103/08/24)
Impression:

1) Suspect **recurrent tumor at the left upper gingiva** (2.4cm@Se/Im: 3/14).

2) Persistent prominent **soft tissue lesion in the lower lip and submandibular area** (Se/Im: 3/18-20). **DDx:** granulation tissue, recurrent tumor. Suggest tissue proof.
1. SCC on lower gingiva cT4cN0M0 stage IV
2. ORN, R’ t Md s/p sequestectomy
3. GERD, gr.B
Working Diagnosis
### Inflammation or Cyst or Neoplasm?

<table>
<thead>
<tr>
<th></th>
<th>Our case</th>
<th>Inflammation</th>
<th>Cyst</th>
<th>Neoplasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>Red</td>
<td>Red</td>
<td>Normal</td>
<td>Variable</td>
</tr>
<tr>
<td>Fever</td>
<td>x</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Consistency</td>
<td>Rubbery</td>
<td>Rubbery</td>
<td>Soft</td>
<td>Firm</td>
</tr>
<tr>
<td>Margin</td>
<td>Irregular</td>
<td>Irregular</td>
<td>Regular</td>
<td>Irregular</td>
</tr>
<tr>
<td>Discharge</td>
<td>x</td>
<td>+</td>
<td>-</td>
<td>+/-</td>
</tr>
<tr>
<td>Pain</td>
<td>x</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Ulceration</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Mobility</td>
<td>Fixed</td>
<td>Fixed</td>
<td>Fluxuation</td>
<td>Fixed</td>
</tr>
<tr>
<td>Duration</td>
<td>A month</td>
<td>Days</td>
<td>Years</td>
<td>Months</td>
</tr>
</tbody>
</table>
“Neoplasma"
<table>
<thead>
<tr>
<th></th>
<th>Our case</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface</td>
<td>Smooth</td>
<td>Smooth</td>
<td>Rough</td>
</tr>
<tr>
<td>Ulceration</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>X-ray margin</td>
<td>X</td>
<td>Well-defined</td>
<td>Poor defined</td>
</tr>
<tr>
<td>Mobility</td>
<td>Fixed</td>
<td>Movable</td>
<td>Fixed</td>
</tr>
<tr>
<td>Duration</td>
<td>A month</td>
<td>Years</td>
<td>Months</td>
</tr>
</tbody>
</table>
Malignant
Central or Peripheral?

"Peripheral"
Differential Diagnosis

1. Squamous cell carcinoma
2. Radiation induced malignant fibrous histiocytoma
3. Neurosarcoma
4. Fibrosarcoma
5. Tuberculosis
# Squamous cell carcinoma

<table>
<thead>
<tr>
<th>Factors</th>
<th>Our case</th>
<th>SCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65</td>
<td>Increasing age</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Site</td>
<td>Left Tongue Border</td>
<td>1. Buccal mucosa</td>
</tr>
<tr>
<td>Duration</td>
<td>A month</td>
<td>4~8 months</td>
</tr>
<tr>
<td>Color</td>
<td>Red</td>
<td>Red/Yellow</td>
</tr>
<tr>
<td>Shape</td>
<td>Irregular</td>
<td>Irregular</td>
</tr>
<tr>
<td>Surface</td>
<td>Smooth</td>
<td>Rough</td>
</tr>
<tr>
<td>Mobility</td>
<td>Fixed</td>
<td>Fixed</td>
</tr>
<tr>
<td>Consistency</td>
<td>Rubbery</td>
<td>Firm</td>
</tr>
<tr>
<td>Pain</td>
<td>x</td>
<td>-</td>
</tr>
<tr>
<td>Induration</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
Radiation induced Malignant fibrous histiocytoma

<table>
<thead>
<tr>
<th>Factors</th>
<th>Our case</th>
<th>Radiation induced Malignant fibrous histiocytoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65</td>
<td>No predilection</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>No predilection</td>
</tr>
<tr>
<td>Site</td>
<td>Left tongue border</td>
<td>No predilection</td>
</tr>
<tr>
<td>Duration</td>
<td>A month</td>
<td>Growing rapidly</td>
</tr>
<tr>
<td>Color</td>
<td>Red</td>
<td>Red</td>
</tr>
<tr>
<td>Shape</td>
<td>Irregular</td>
<td>Irregular</td>
</tr>
<tr>
<td>Surface</td>
<td>Smooth</td>
<td>Rough</td>
</tr>
<tr>
<td>Mobility</td>
<td>Fixed</td>
<td>Fixed</td>
</tr>
<tr>
<td>Consistency</td>
<td>Rubbery</td>
<td>Firm</td>
</tr>
<tr>
<td>Pain</td>
<td>x</td>
<td>-</td>
</tr>
<tr>
<td>Induration</td>
<td>+</td>
<td>+</td>
</tr>
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</table>
# Neurosarcoma

<table>
<thead>
<tr>
<th>Factors</th>
<th>Our case</th>
<th>Neurosarcoma</th>
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<tbody>
<tr>
<td>Age</td>
<td>65</td>
<td>20~50</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>No predilection</td>
</tr>
<tr>
<td>Site</td>
<td>Left tongue border</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. Tongue</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. the floor of mouth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. palate</td>
</tr>
<tr>
<td>Duration</td>
<td>A month</td>
<td>Slow growing</td>
</tr>
<tr>
<td>Color</td>
<td>Red</td>
<td>Red</td>
</tr>
<tr>
<td>Shape</td>
<td>Irregular</td>
<td>Nodule / dome, solitary</td>
</tr>
<tr>
<td>Surface</td>
<td>Smooth</td>
<td>Smooth</td>
</tr>
<tr>
<td>Mobility</td>
<td>Fixed</td>
<td>Movable to fixed</td>
</tr>
<tr>
<td>Consistency</td>
<td>Rubbery</td>
<td>Elastic tight</td>
</tr>
<tr>
<td>Pain</td>
<td>x</td>
<td>-</td>
</tr>
<tr>
<td>Induration</td>
<td>+</td>
<td>+</td>
</tr>
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</table>
### Fibrosarcoma

<table>
<thead>
<tr>
<th>Factors</th>
<th>Our case</th>
<th>Fibrosarcoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65</td>
<td>Any age (Most in young adult and children)</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>Male : Female = 1 : 1</td>
</tr>
<tr>
<td>Site</td>
<td>Left tongue border</td>
<td>Extremities ; Neck and Head (10%)</td>
</tr>
<tr>
<td>Duration</td>
<td>A month</td>
<td>Slow growing</td>
</tr>
<tr>
<td>Color</td>
<td>Red</td>
<td>Normal</td>
</tr>
<tr>
<td>Shape</td>
<td>Irregular</td>
<td>Irregular</td>
</tr>
<tr>
<td>Surface</td>
<td>Smooth</td>
<td>Rough</td>
</tr>
<tr>
<td>Mobility</td>
<td>Fixed</td>
<td>Fixed</td>
</tr>
<tr>
<td>Consistency</td>
<td>Rubbery</td>
<td>Firm</td>
</tr>
<tr>
<td>Pain</td>
<td>x</td>
<td>+</td>
</tr>
<tr>
<td>Induration</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
# Tuberculosis

<table>
<thead>
<tr>
<th>Factors</th>
<th>Our case</th>
<th>Tuberculosis</th>
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</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>65</td>
<td>Primary: Unspecified</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>Female</td>
<td>Secondary: Old age</td>
</tr>
<tr>
<td><strong>Site</strong></td>
<td>Left tongue border</td>
<td>Tongue, Palate, Lip</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gingiva, Mucobuccal fold</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>A month</td>
<td>months</td>
</tr>
<tr>
<td><strong>Color</strong></td>
<td>Red</td>
<td>Yellow</td>
</tr>
<tr>
<td><strong>Shape</strong></td>
<td>Irregular</td>
<td>Irregular</td>
</tr>
<tr>
<td><strong>Surface</strong></td>
<td>Smooth</td>
<td>Rough</td>
</tr>
<tr>
<td><strong>Mobility</strong></td>
<td>Fixed</td>
<td>Fixed</td>
</tr>
<tr>
<td><strong>Consistency</strong></td>
<td>Rubber</td>
<td>Firm</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td>x</td>
<td>+</td>
</tr>
<tr>
<td><strong>Induration</strong></td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>
Clinical impression

“Malignant neoplasm of tongue, unspecified”
**Treatment course**

**Surgery (103/08/26)**

1. Routine patient identification check and time out
2. Patient was put in supine position, GA with NETT intubation
3. Routine aseptic and OMS draping procedures were done
4. Prophylactic antibiotic: Cefazolin (1g) 1 vial + Aq-dest 20 ml IV was injected.
5. Throat pack in and OP started
**Treatment course**

**Surgery (103/08/26)**

6. **Tumor debulking:**
   1) excision of main portion of lesion over L’t tongue border
   2) Remove part of lesion over L’t palate (ant.)
   3) Specimen sent for H-P exam

7. Wound packing with gelfoam and bosmin gauze

8. Throat pack out and OP ended

9. N-G placement
Treatment course

Pre-OP

Post-OP
Histopathology report

組織名稱：Tongue border, left
臨床診斷：Squamous cell carcinoma (second-primary)
腫瘤代碼：(M-8801/3)

Pathologic diagnosis:
Oral cavity, tongue border, left, incision, sarcoma, suggestive of malignant fibrous histiocytoma

Gross Examination:
The specimen submitted consists of 1 soft tissue fragment in 1 bottle, measuring 0.5 x 0.5 x 0.3 cm in size, fixed in formalin. Grossly, it is whitish in color and rubbery in consistency.
Microscopic Examination:
The slide contains two identical groups of irregular-shaped soft tissue specimens. Microscopically, it is characterized by a sheet of diffuse poorly differentiated, bizarre, pleomorphic multinucleated, spindle-shaped neoplastic cells underlying a large area of necrotic tissue. Immunohistochemical stainings of vimentin and CD68 show diffuse strong positive staining for the neoplastic cells; cytokeratin shows negative staining for the neoplastic cells.

Based upon the above findings, it shows sarcoma, suggestive of malignant fibrous histiocytoma.

◆ The pathologic diagnosis has been concurred by peer slide review.
Discussion-

Radiation Induced Sarcoma of Oral Cavity-
A Rare Case Report and a Short Review

Journal of Clinical and Diagnostic Research.
2013 Nov, Vol-7(11)
Sivaraman Ganesan, Elizabeth Mathew Iype, Aravind S. Kapali, and Renu S.
Radiation - Induced Sarcoma (RIS) are rare clinical entity. They arise from previously irradiated areas and have a prolonged latency period.
Abstract

- Radiation-induced sarcoma in a 67–year–old male
- Involve left Retromolar Trigone region
- Squamous cell carcinoma of tongue
- Wide excision, neck dissection and post-operative radiation
Case Report

- A 67 year male patient
- Reported to Head and Neck Surgery OPD on Feb. 2013
- History of a swelling on the left side of the oral cavity for the past 1 year
- Insidious in onset, progressively increasing
- No pain or difficulty in opening the mouth.
- No history of neck swellings, voice change or respiratory difficulty
Well differentiated SCC of the tongue, T2N0M0

Underwent wide excision of left lateral tongue with

Followed by post-operative radiation of 50 Gy in 15 fractions at November 1994

on regular follow-up and detected this swelling presently.
Case Report

a large 4 x 4cm exophytic, reddish irregular polypoidal mass in the left retromolar trigone (RMT) region with areas of ulceration
Palpation mass was firm/ non-tender / pedunculated

No other significant lesion in the oral cavity

Initial operated site was normal

No regional lymphadenopathy was noted.
Case Report

- Pedunculated / 2.7x 2x 2.5 cm/in the oropharynx
- Probably from left palatoglossal fold, into left tonsillar fossa.
- Soft & hard palate not involved / abutting medial pterygoid m.
Lined by hyperplastic squamous epithelium with sub-epithelium demonstrating infiltrating neoplasm composed of pleomorphic cells.
Cytokeratin, EMA, HMB45 were negative, whereas Vimentin (mesenchymal tissue marker) and S-100 protein (nerve fiber) were strongly positive.
Treatment option of radical surgery with reconstruction was explained to the patient.

As the patient wanted to be on follow up, he is being followed up regularly.
Radiation induced sarcoma: rare (0.16%), poor prognosis

Diagnosis of RIS (1948, Cahan et al.):
- sarcoma must develop within the boundaries of a previously irradiated area
- relatively long asymptomatic latent period (at least 4 years) must have elapsed
- sarcoma must have a different histology from the original lesion
- sarcoma must be histologically confirmed
Diagnosis of RIS (1999, Murray et al.):
- history of irradiation with the sarcoma arising in the area included in the radiation field and the 5% isodose line
- no evidence that the sarcoma was present before the radiation therapy
- sarcomas must be proven histologically and be of different pathology compared with the primary tumor

The latency period for development of RIS is typically 5–20 years

-> Our patient: 18 years
Risk factors for developing RIS:
- young age at treatment
- high radiation dose
- simultaneous chemotherapy with alkylating agents

Radiation above 50 Gy cause cell death, while lower doses (<30Gy) cause genomic instability and damage cell repair mechanisms. RIS typically occur within or at the edges of the radiation field.

→ Our patient: 50 Gy in y/o, didn’t receive any chemotherapy.
Familial gastrointestinal stromal tumor syndrome (GIST), Li-Fraumeni syndrome, retinoblastoma, Werner syndrome, Neurofibromatosis Type 1, Costello Syndrome, and Nijmegen breakage syndrome are associated with increased risk of bone or soft tissue sarcoma, along with multiple other tumors.

-> Our patient did not undergo any genetic testing.
Surgery is the standard treatment for RIS. It is very difficult for complete resection because of its proximity to vital organs in the head and neck. The prognosis of patients with incompletely excised tumors is much worse than that of patients with no residual tumor because of tumor insensitivity to chemo-and radiotherapy.
Emphasise the proper investigations based on the patient’s history & symptoms, especially the appearance or a change in the irradiated area, which can lead to an early diagnosis.
醫學倫理討論
Tom Beauchamp & James Childress
六大原則 - 1979

1. 生命的神聖性(Sanctity of life)：
2. 行善原則(Beneficence)：醫師要盡其所能延長病人之生命且減輕病人之痛苦。
3. 誠信原則(Veracity)：醫師對其病人有「以誠信相對待」的義務。
4. 自主原則(Autonomy)：病患對其己身之診療決定的自主權必須得到醫師的尊重。
5. 不傷害原則(Nonmaleficence)：醫師要盡其所能避免病人承受不必要的身心傷害。
6. 保密原則(Confidentiality)：醫師對病人的病情負有保密的責任。
7. 公義原則(Justice)：醫師在面對有限的醫療資源時，應以社會公平、正義的考量來協助合理分配此醫療資源給真正最需要它的人。
生命的神聖性

“在《聖經》的第一篇<創世紀>中，上帝告訴以色列人說:「上帝按他自己的形象造人。」「你將是神聖的，因為我是神聖的。」「生命神聖」觀即由此衍生而得。

該觀點主張人的生命是無條件的，有價值及神聖的，人繼承了上帝的品質，包括一切價值的來源-內具的善（intrinsic goodness），因此必須受到尊重。

藉此瞭解他個人生命的原真，而認知他個人存活在世上的主要工作和生活的目的，找到個人存在的意義、價值、目的與任務。
行善原則

“R/T可能會導致腫瘤發生，那病人是否真的需要進行R/T治療？或是只是增加病人的痛苦。
→儘管R/T可能會導致病人腫瘤的發生，但其機率就統計而言還是偏低的。但若病人原腫瘤無法藉由手術完全切除，R/T還是有其進行的必要性，如此才能真正清除病兆。
誠信原則

“對於患者的疾病嚴重程度是否有確實地通知，盡到告知的義務？

“是否有清楚的向病人說明清楚疾病病程、治療計畫、預後、風險？

→皆以已告知病人後，經同意才進行手術。
自主原則

“充分說明病情及治療計畫、風險之後，是否有讓病人充分自主地選擇治療計畫？
→病人及家屬選擇並同意醫師的建議。

“在做全身麻醉以前，是否有說明完整之後再請病人自主的簽名同意？
→已充分說明並與家屬溝通，並簽名同意。”
不傷害原則

是否有先完整瞭解病人的病史?
→治療前有完整蒐集病史資料，並與病患溝通後擬定進一步的治療計畫

手術過程中，是否有造成不必要的醫源性的傷害？
→沒有不必要醫源性傷害。
保密原則

告知的對象

1. 本人為原則
2. 病人未明示反對時，亦得告知其配偶與親屬
3. 病人為未成年人時，亦須告知其法定代理人
4. 若病人意識不清或無決定能力，應須告知其法定代理人、配偶、親屬或關係人
5. 病人得以書面敘明僅向特定之人告知或對特定對象不予告知
公義原則

手術的必要性？
→Malignant fibrous histiocytoma被視為較有侵犯性的腫瘤，所以應該要大範圍的切除，並且復發機會高，必須搭配C/T完整清除病灶。
醫學倫理總結

在病例撰寫方面(病兆描述，治療計畫，病人態度)應書寫詳盡，使治療過程有詳實的記錄及治療順利。

在進行治療之前，須請病人簽屬同意書

應在不違反醫學倫理的原則之下進行治療的行為
• Oral and maxillofacial pathology Third addition
• Pre-OP of KMUH OS-dept
• http://www.yct.com.tw/life/96lift/96brainstorm06.pdf
• http://www.ncbi.nlm.nih.gov/pmc/articles/PMC387988
doi: 10.7860/JCDR/2013/7351.3624
PMCID: PMC3879883
THANK YOU FOR YOUR ATTENTION!