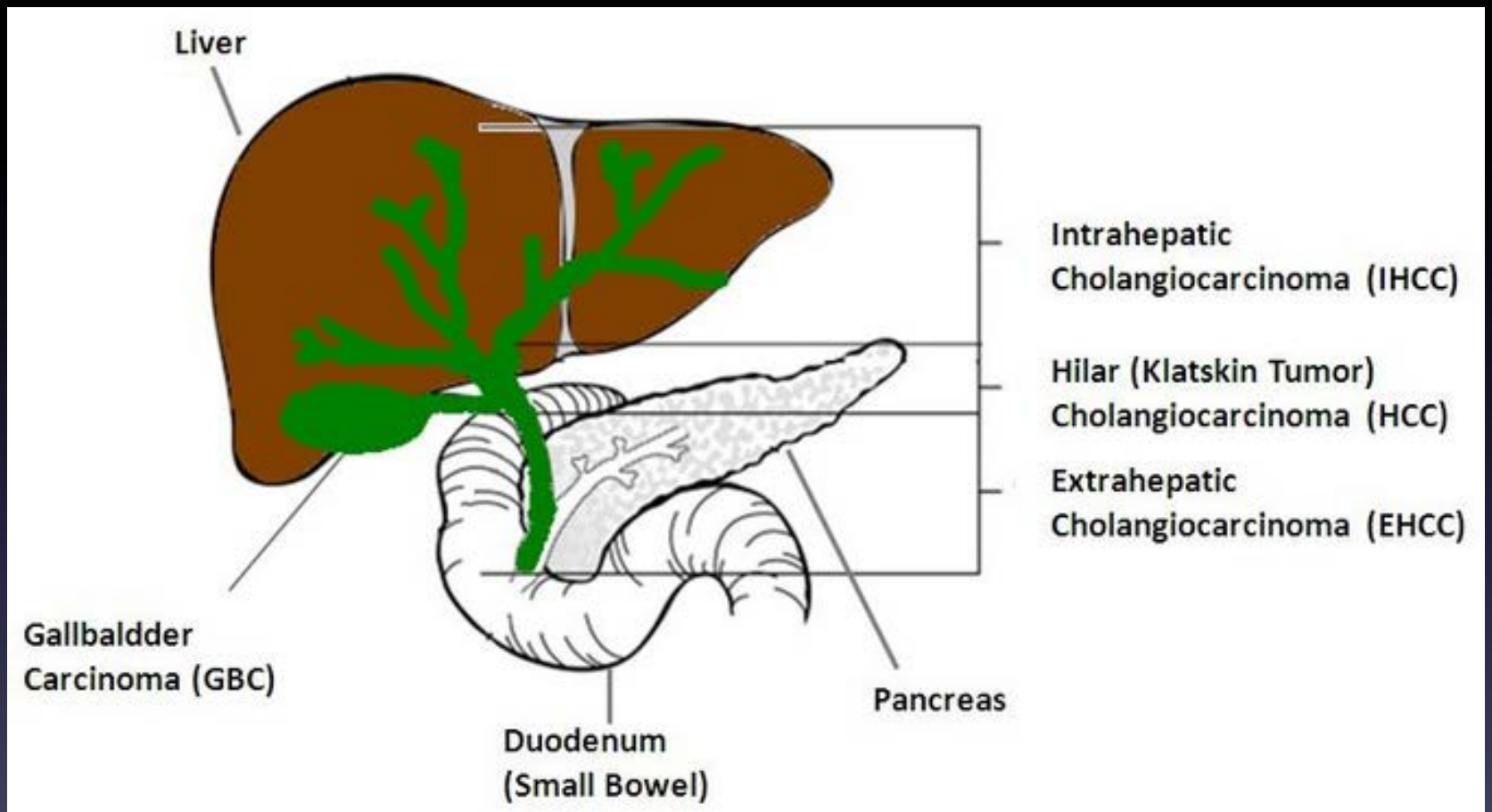


膽胰癌的放射線治療

王嘉雋醫師

台大醫院雲林分院腫瘤醫學部放射腫瘤科

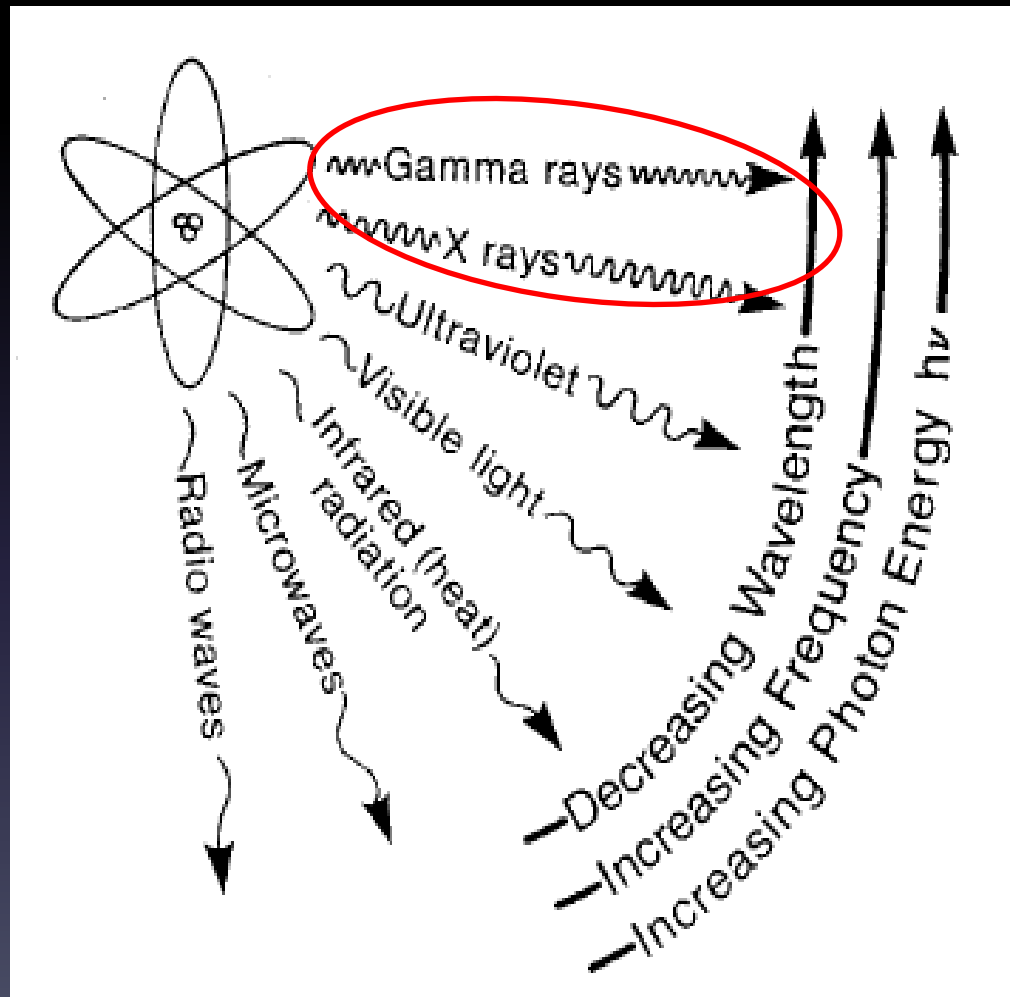


膽胰癌的治療

- 手術治療 
- 全身性治療
- 放射線治療 (Radiotherapy)

什麼是放射線？

電磁波 (輻射)



游離輻射

- 電磁波

- X光 (直線加速器)
- Gamma rays (放射性同位素)

- 粒子射線

- 電子、質子、中子、 α 粒子、 β 粒子.....
- 重粒子 (heavy charged particles)

為何放射線可以殺死癌細胞？

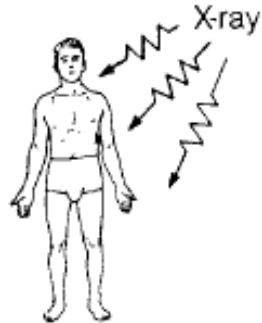
放射線生物效應並不是靠「能量」

Total-Body Irradiation

Mass = 70 kg
 LD/50/60 = 4 Gy
 Energy absorbed =

$$70 \times 4 = 280 \text{ joules}$$

$$= \frac{280}{4.18} = 67 \text{ calories}$$



X-ray

A

Drinking Hot Coffee

Excess temperature (°C) = 60° - 37° = 23°
 Volume of coffee consumed to equal the energy in the LD/50/60 = $\frac{67}{23}$
 = 3 mL
 = 1 sip



B

Mechanical Energy: Lifting a Person

Mass = 70 kg
 Height lifted to equal the energy in the

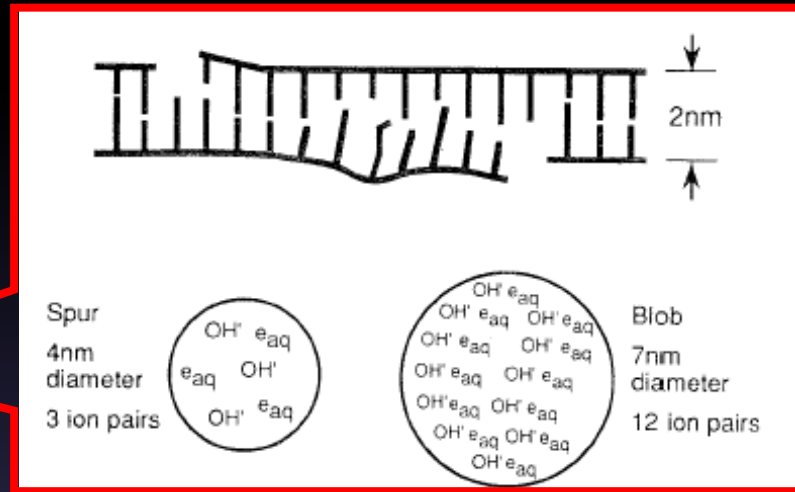
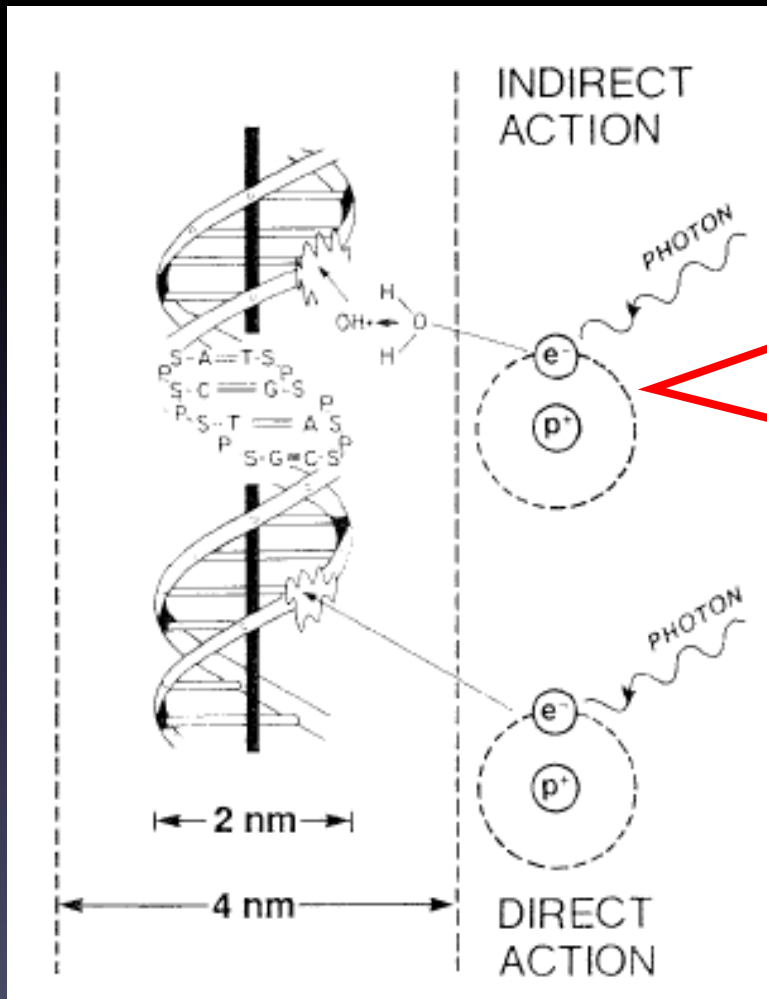
$$LD/50/60 = \frac{280}{70 \times 0.0981}$$

$$= 0.4 \text{ m (16 inches)}$$

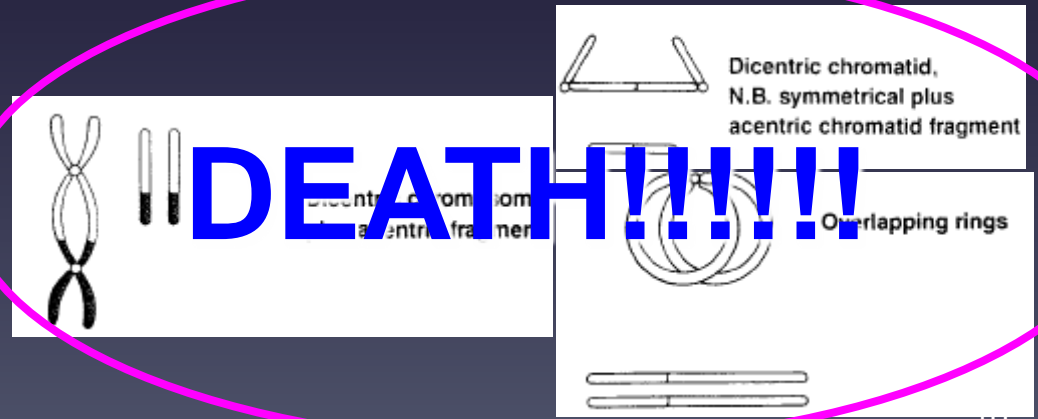
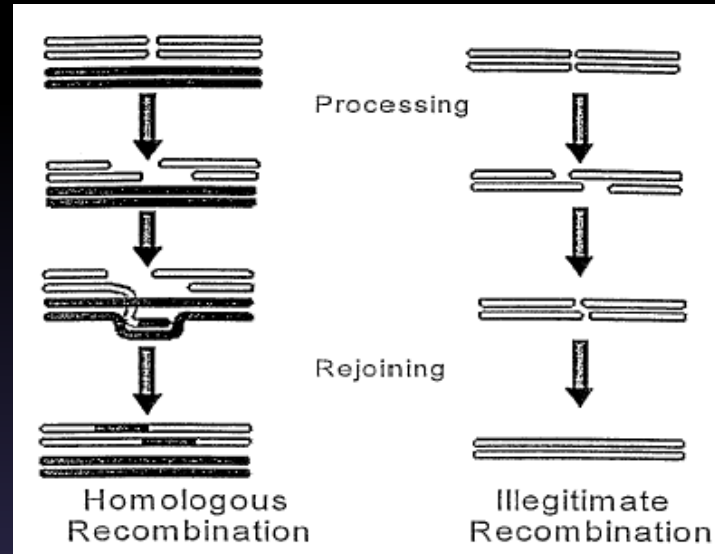
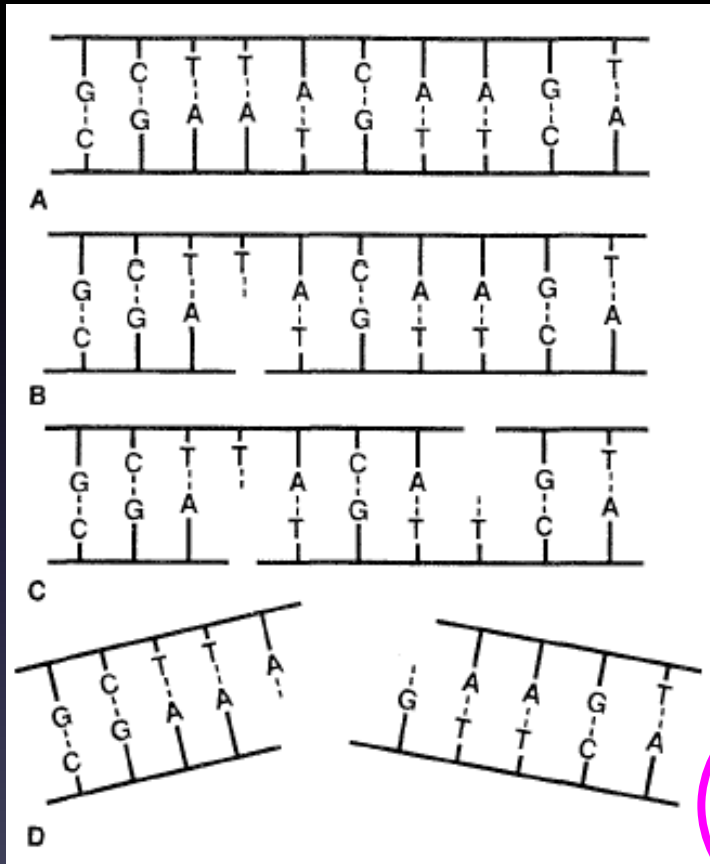


C

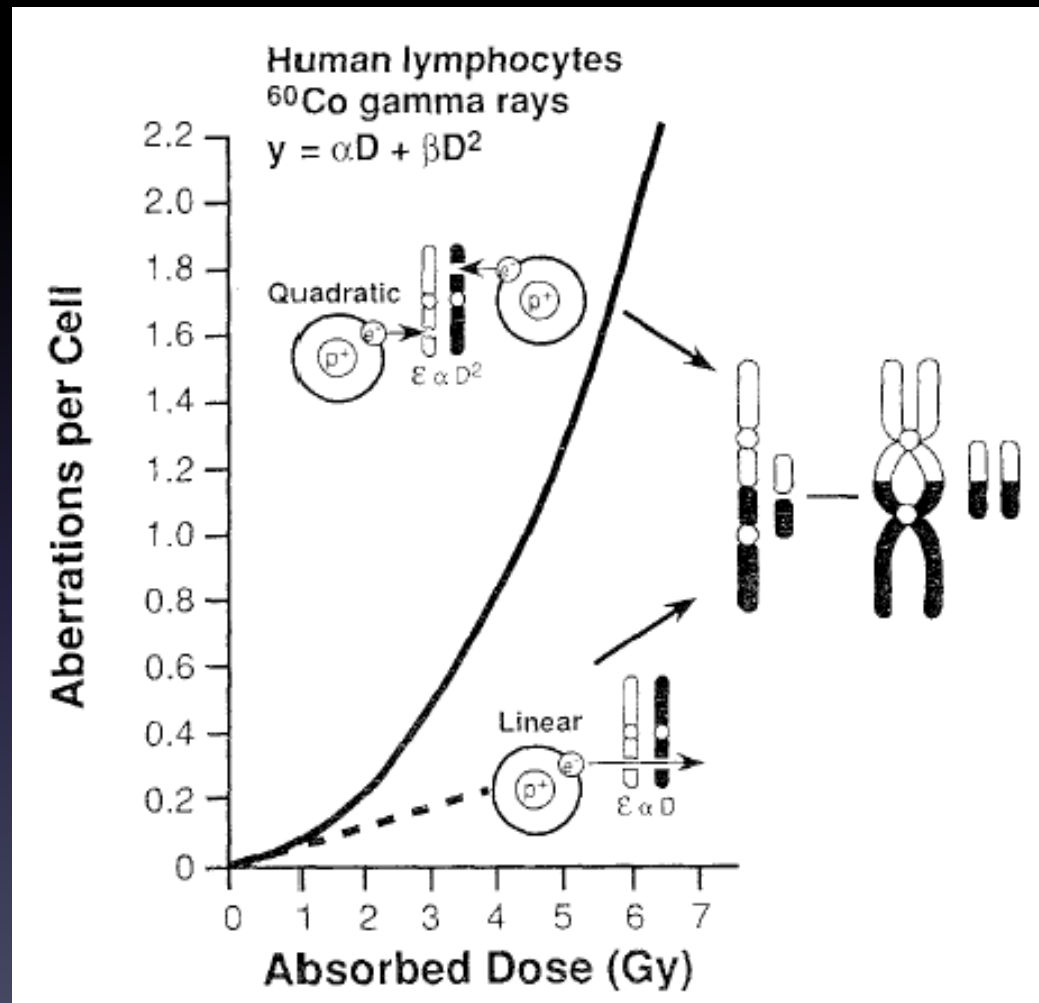
DNA是被攻擊的目標



DNA的修復能力是關鍵



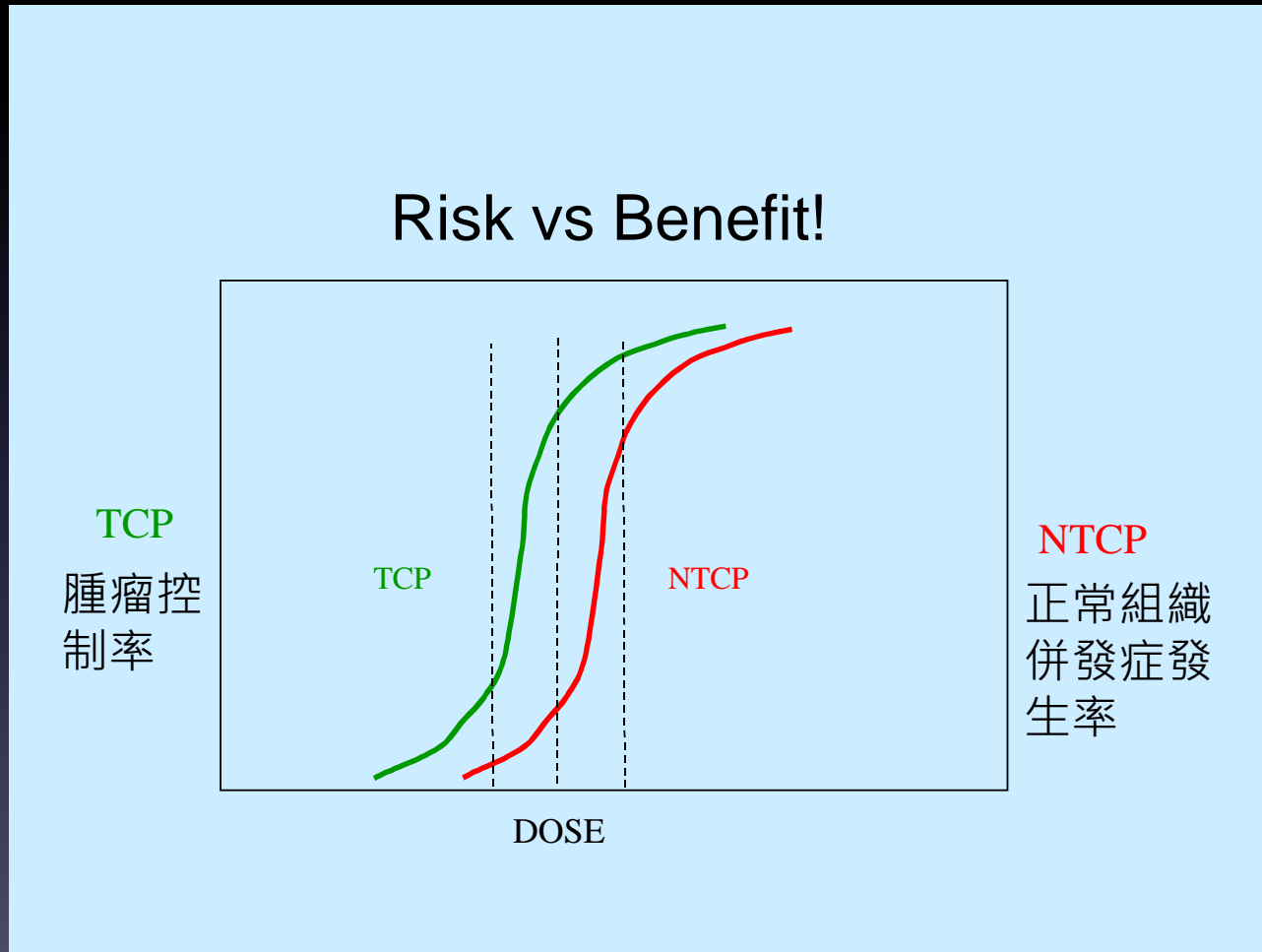
吸收劑量越高，發生染色體變異的機會越大



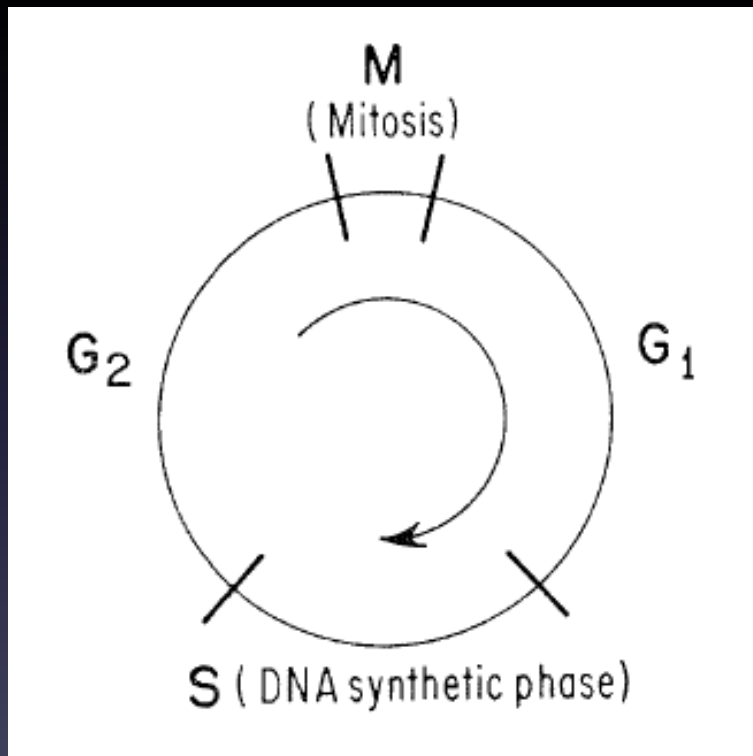
那，為何不一次把劑量統統給完？

Fractionation (分次治療)

1. 要保護正常細胞 (Repair of sublethal damage & Repopulation)



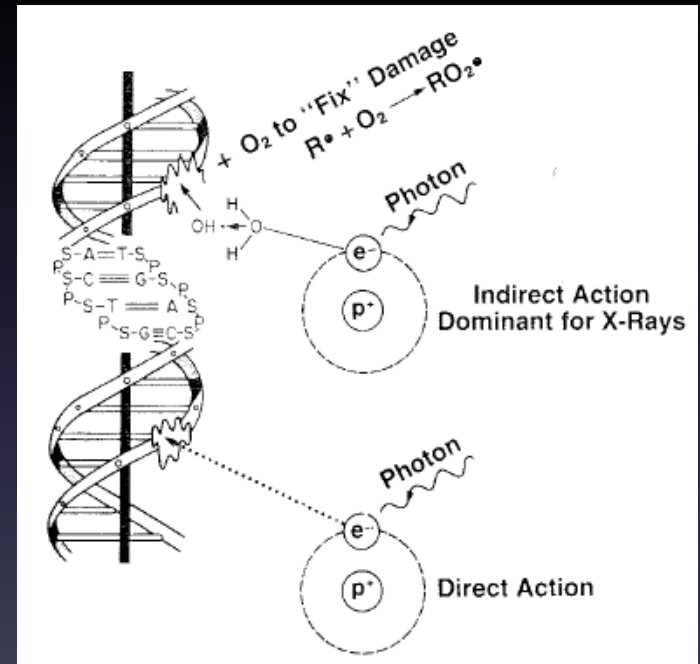
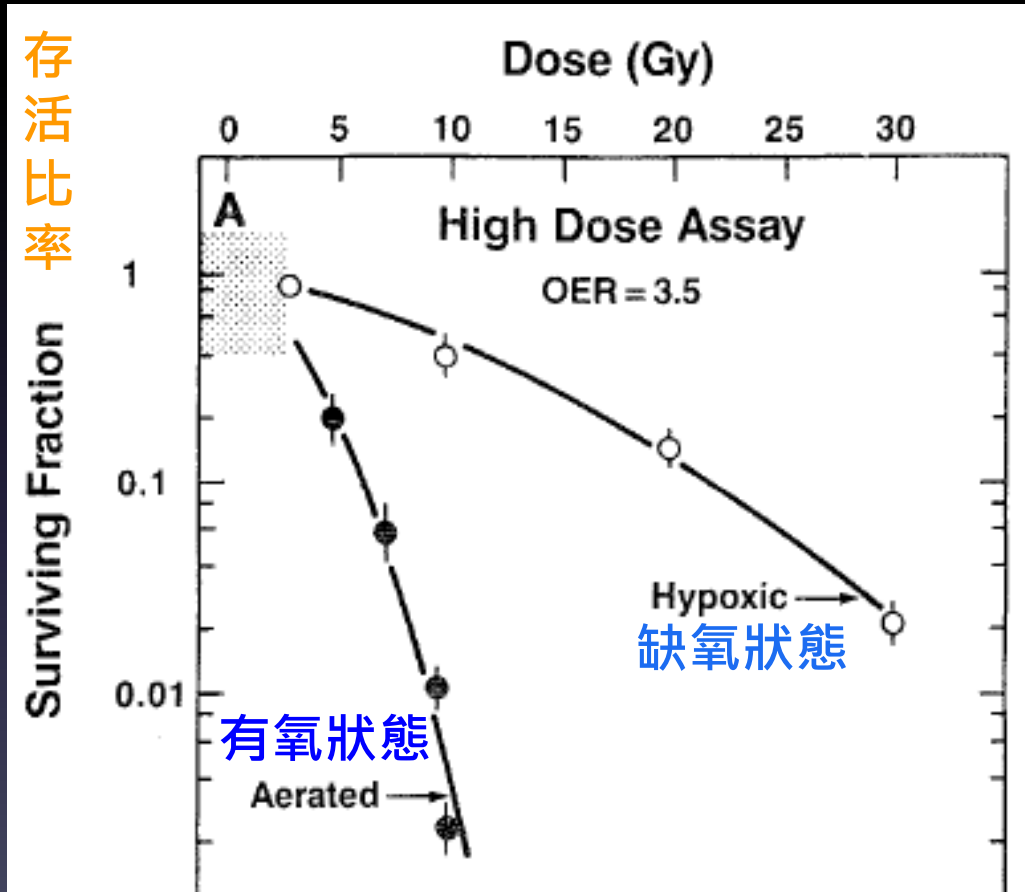
2. 細胞週期再分佈 (Reassortment of cells within the cell cycle)

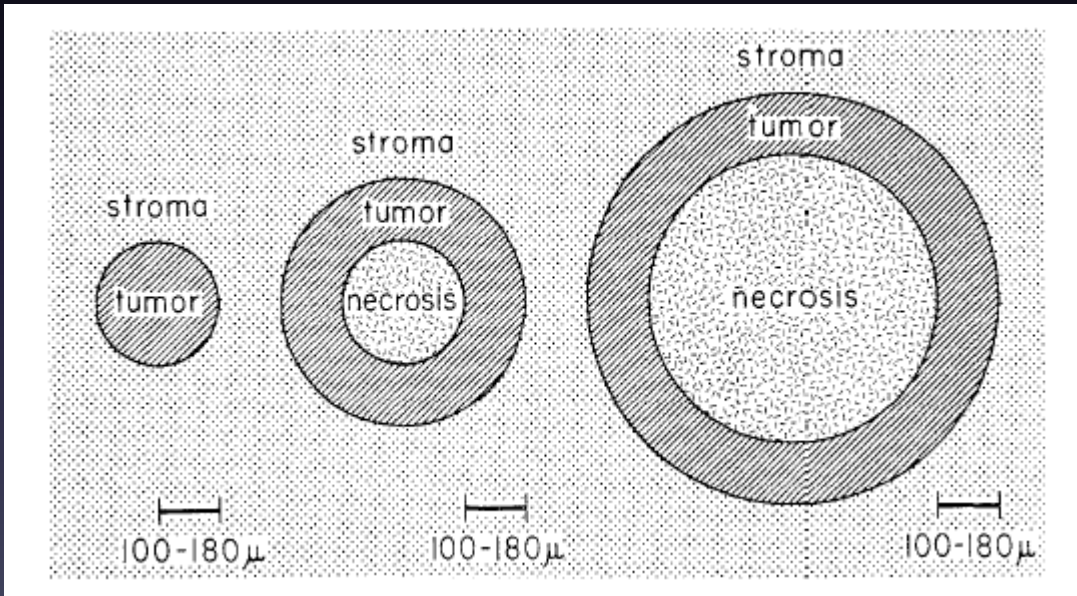
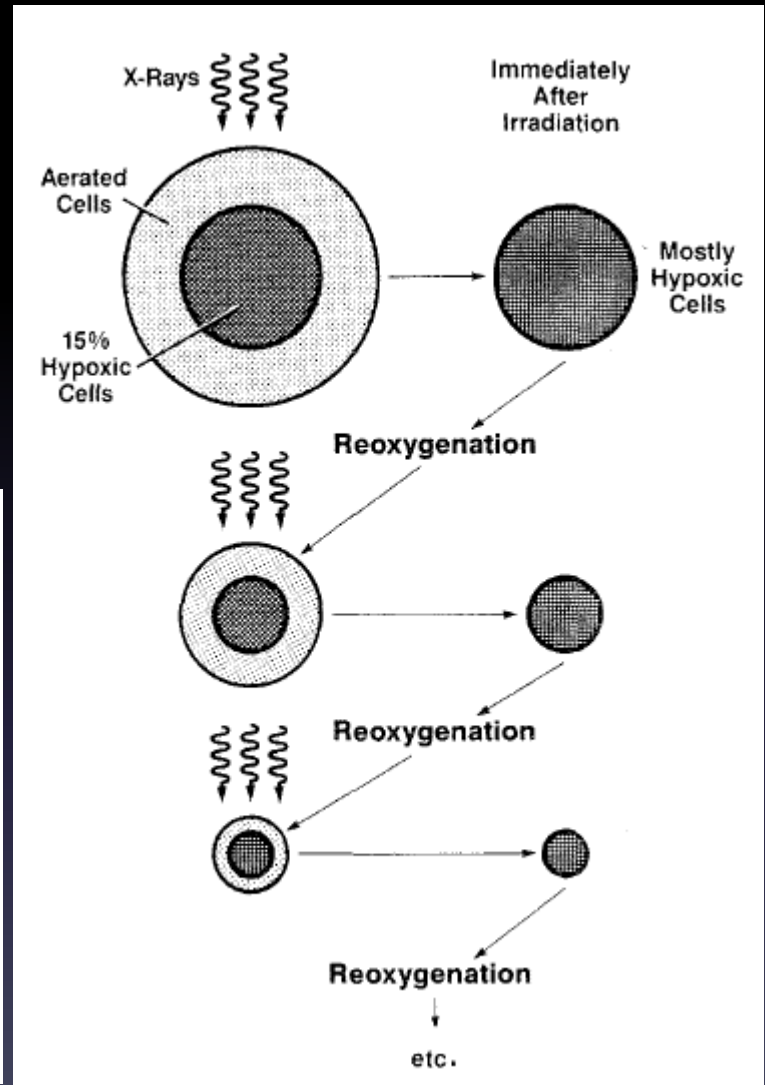
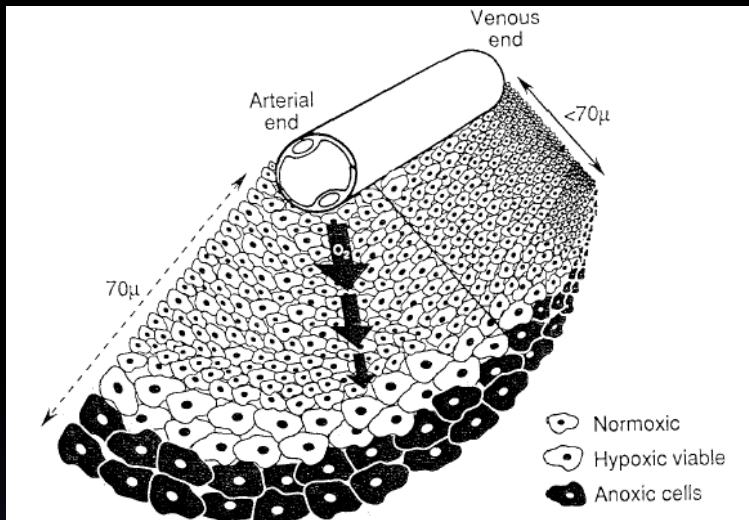


對放射線敏感：
G₂, M (細胞分裂期)

對放射線有抵抗力：
S (DNA合成期) 後期

3. 讓細胞有氧可以加強治療效果 (Reoxygenation)





膽胰癌放射治療的適應症

膽管癌放射治療適應症

- 針對可手術的病人
 - 術後輔助性放射化學治療
 - 尤其是微觀殘餘腫瘤的狀況
- 針對不可手術的病人
 - 根治性/緩解性放射化學治療

胰臟癌放射治療適應症

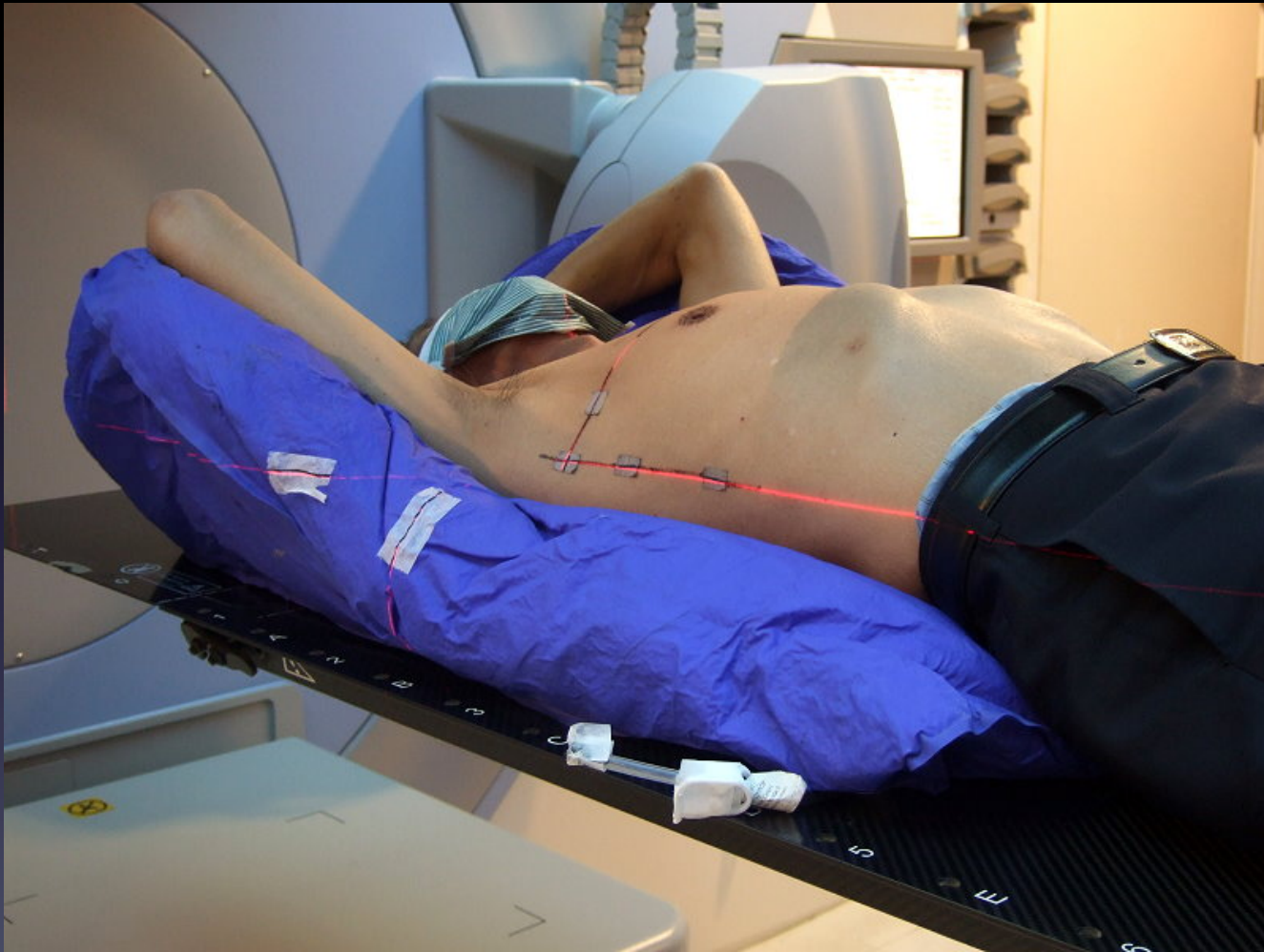
- 針對可手術的病人
 - 術後輔助性放射化學治療
 - 尤其是微觀殘餘腫瘤的狀況
- 針對有機會由無法手術變為可手術的病人
 - 術前輔助性放射化學治療
- 針對不可手術的病人
 - 根治性/緩解性放射化學治療

放射治療的流程

醫療團隊

- 醫師：提供病人癌症諮詢、評估是否適合放射治療、決定治療範圍及計畫、醫療照顧
- 物理師/劑量師：治療劑量的計算及驗證、治療機器的品質保證及安裝、輻射防護業務、新治療技術研發
- 放射師：模具製作、模擬攝影定位、治療機器的操作
- 護理師：病人護理照顧及衛教、協助侵入性醫療行為

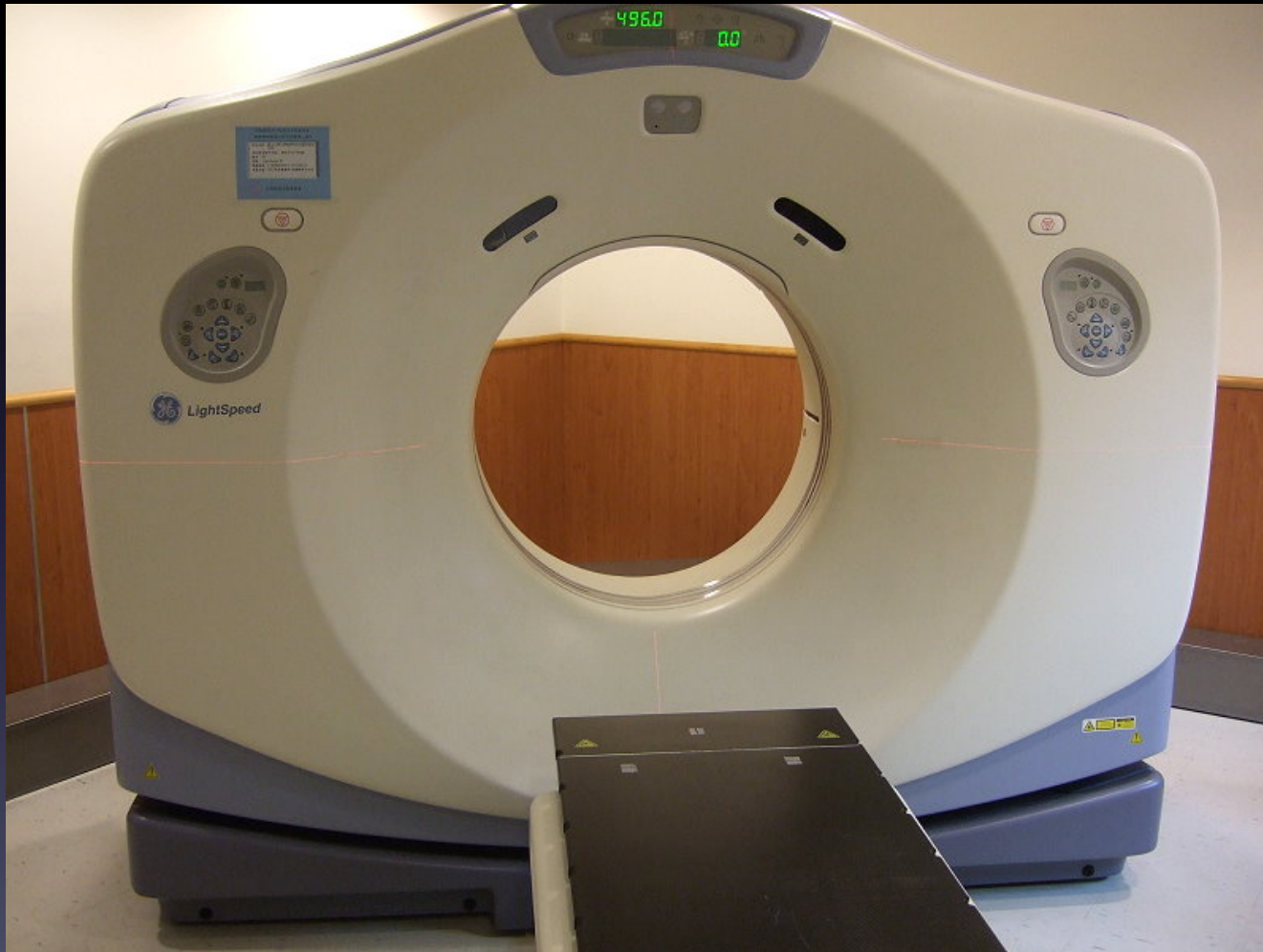
1.A. 製作固定器具



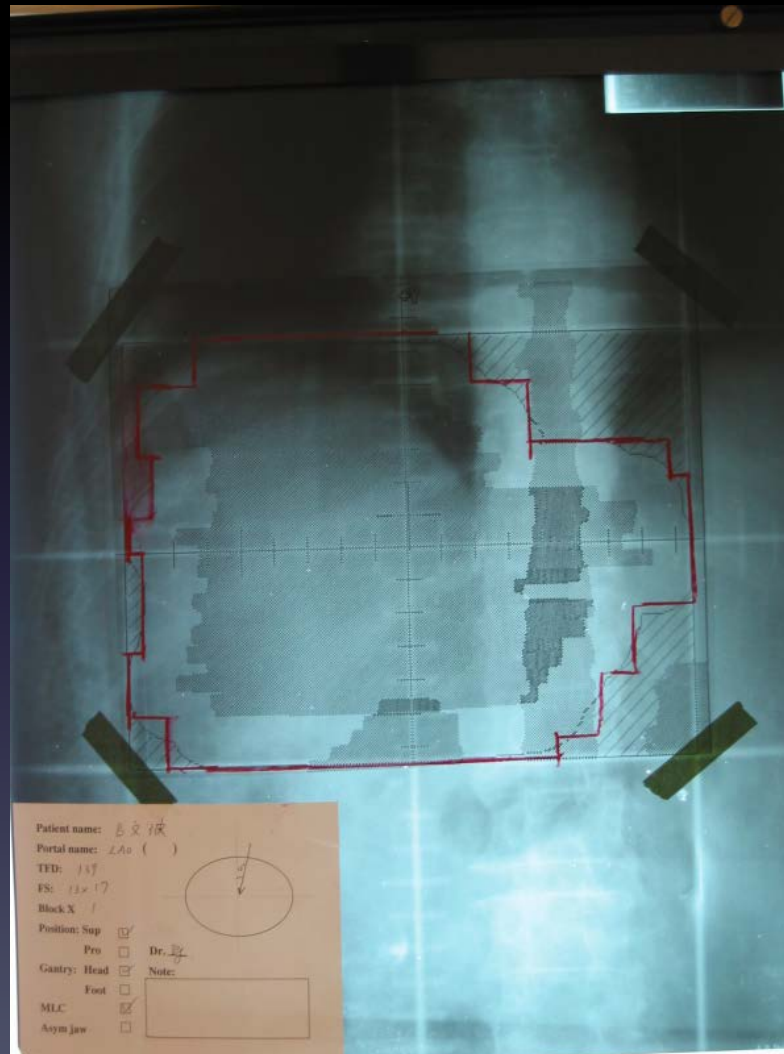
1.B. X光模擬攝影定位



1.C. 電腦斷層攝影

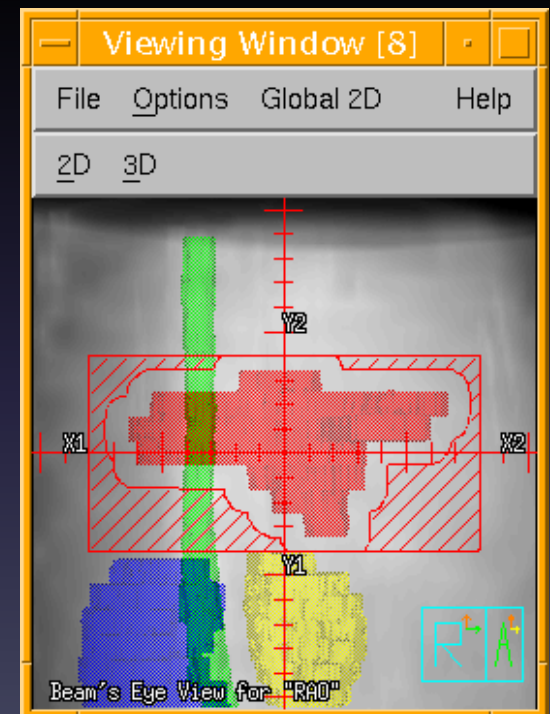
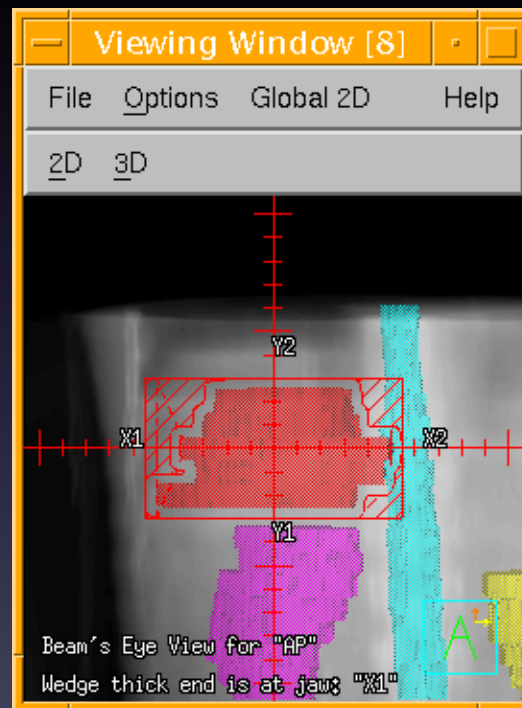
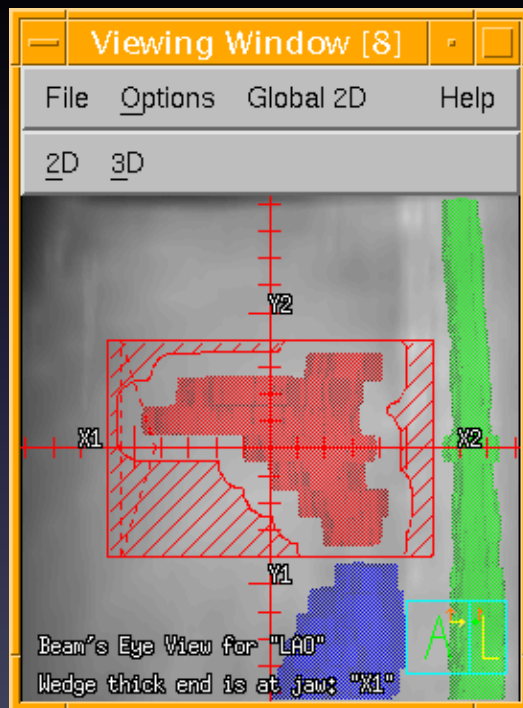


2.A. 傳統治療計畫擬定

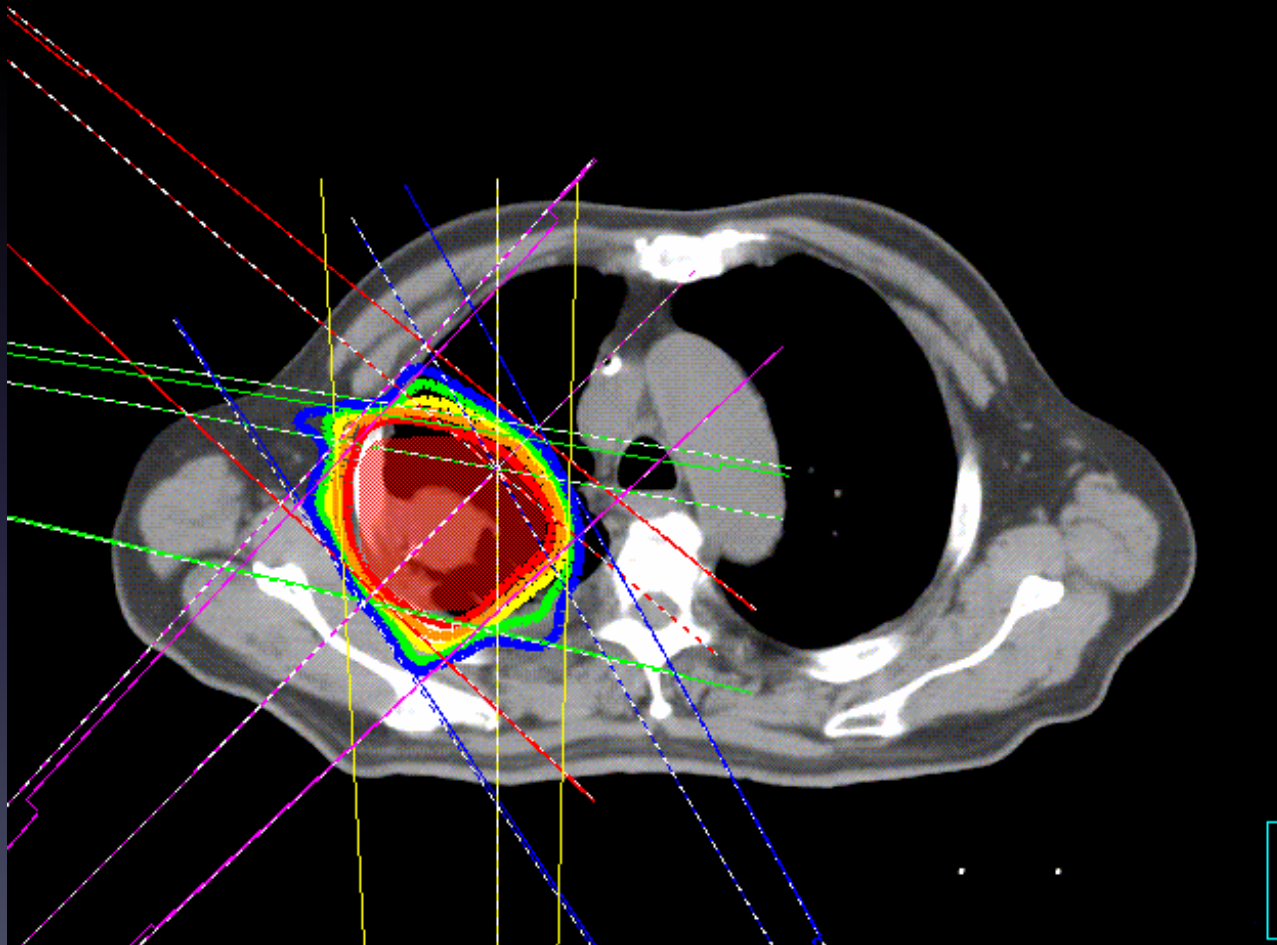


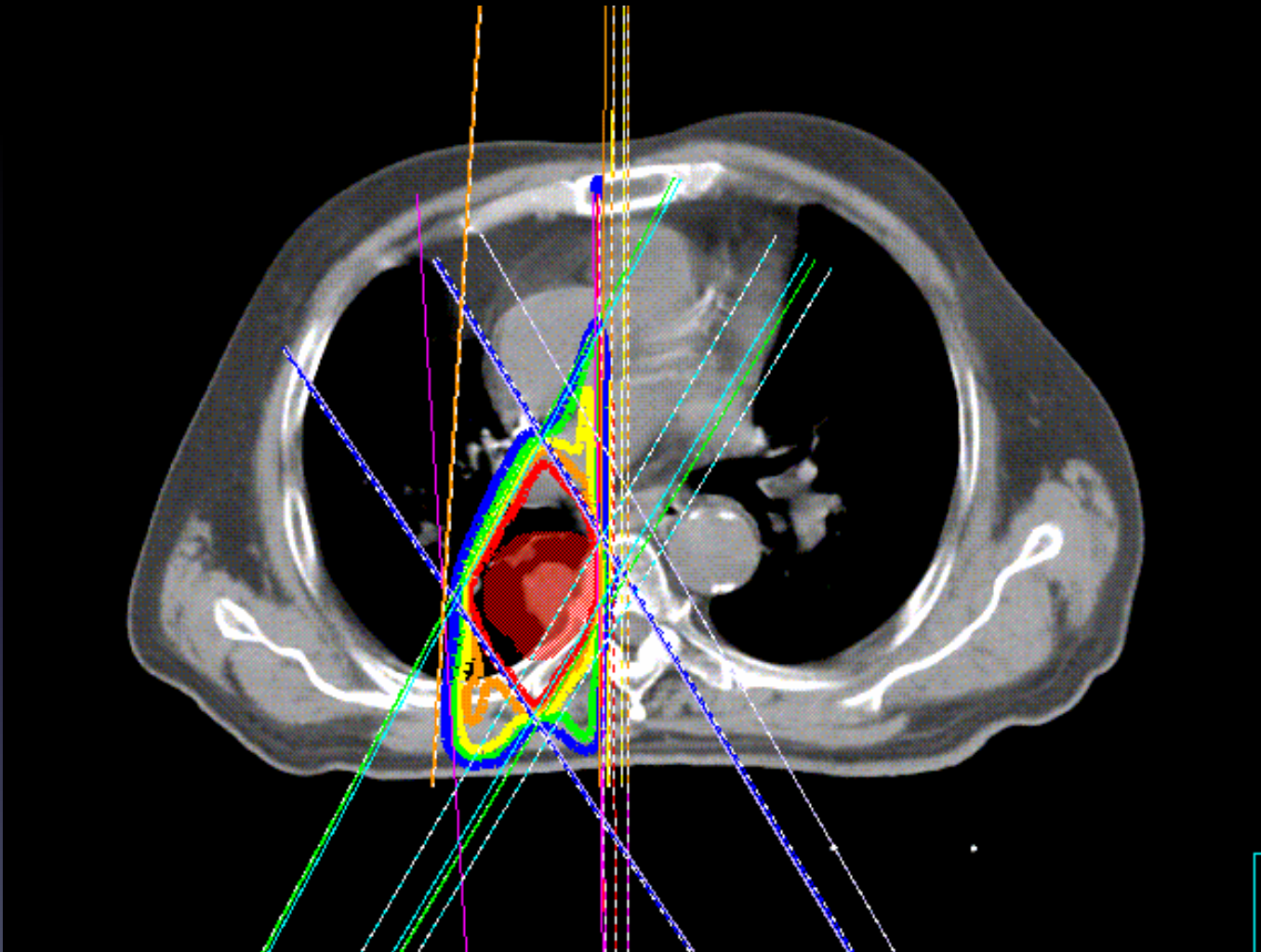
2.B. 電腦治療計畫擬定

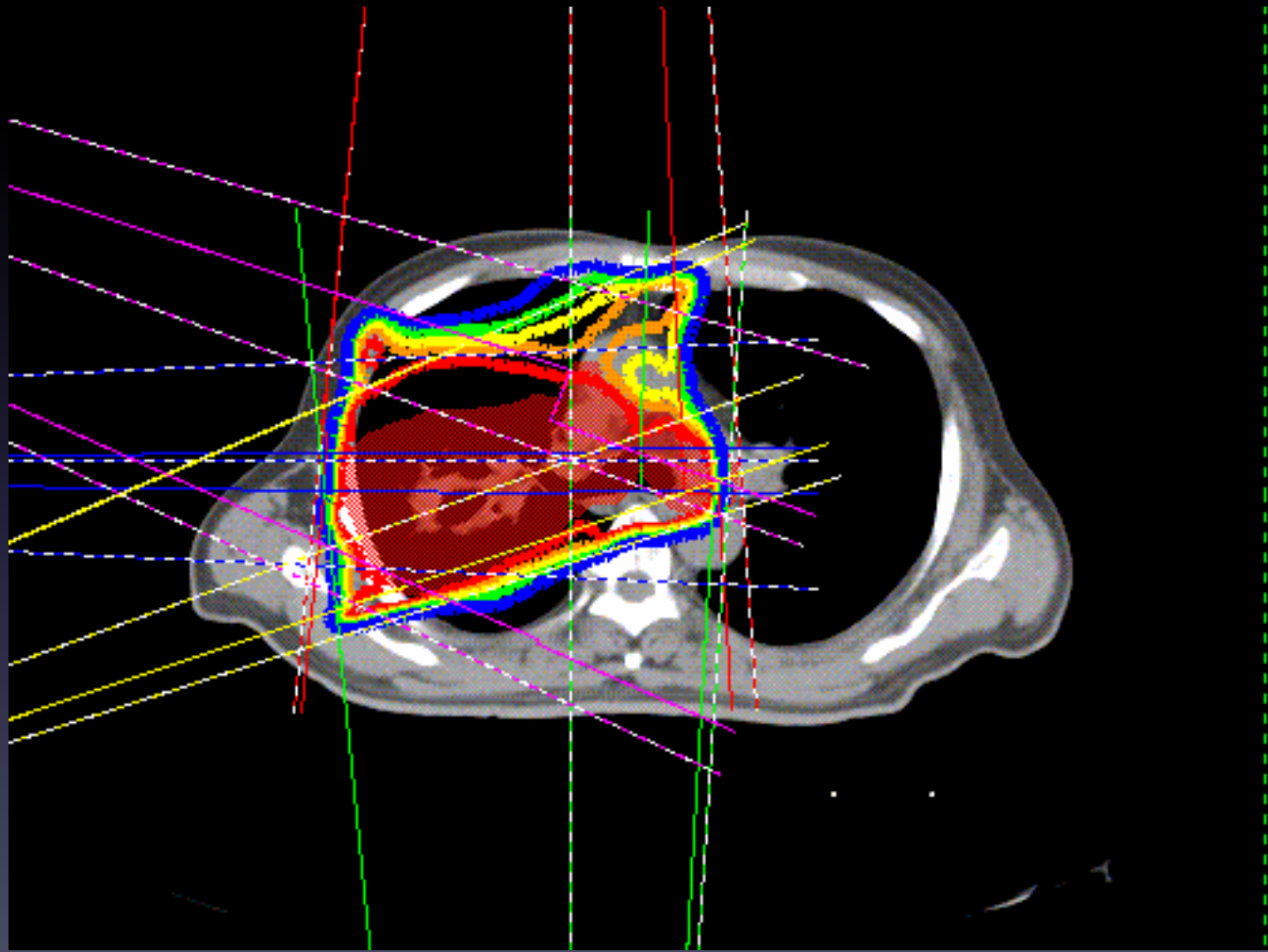
Beam's eye view



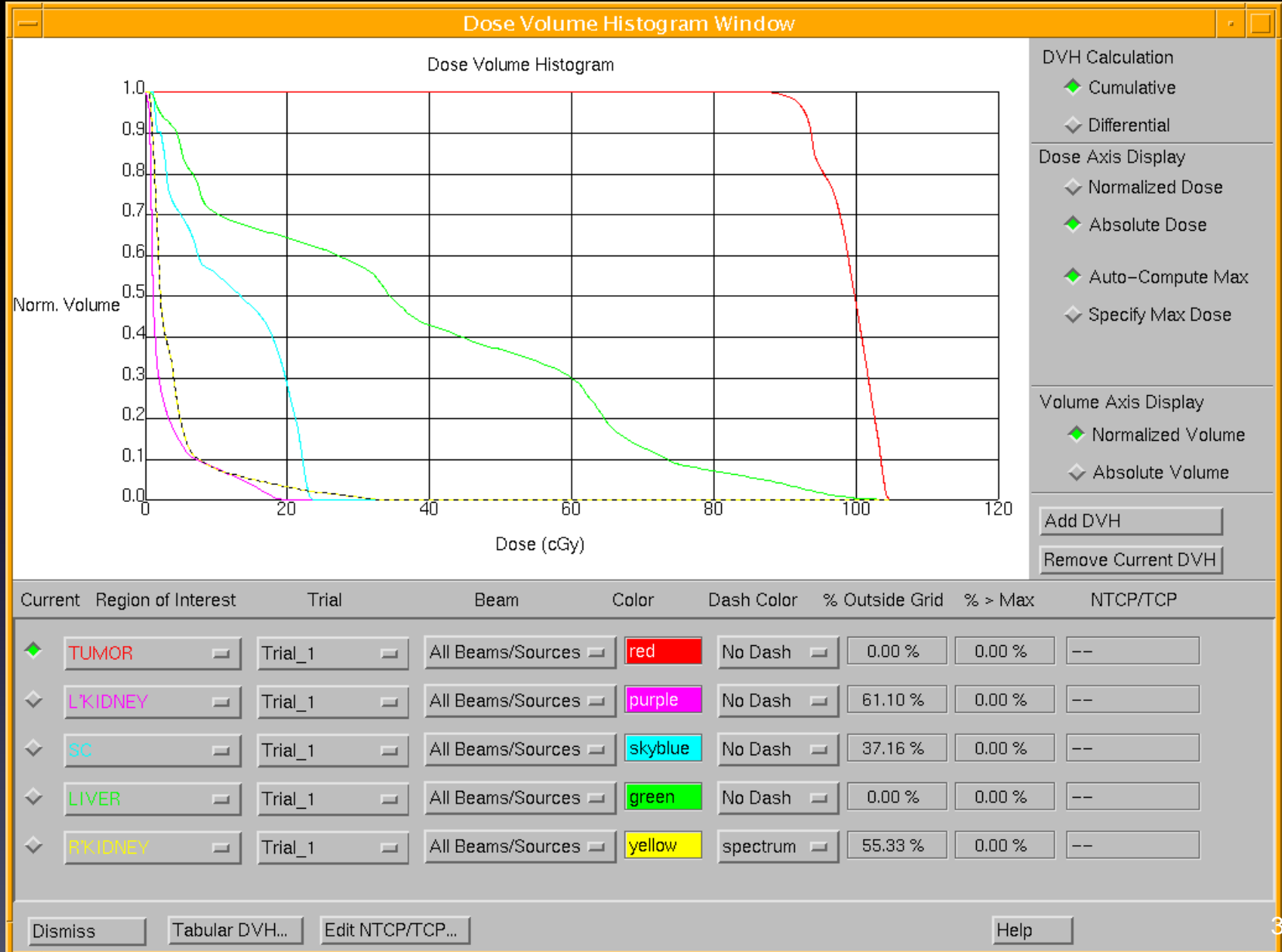
2.B. 電腦治療計畫擬定



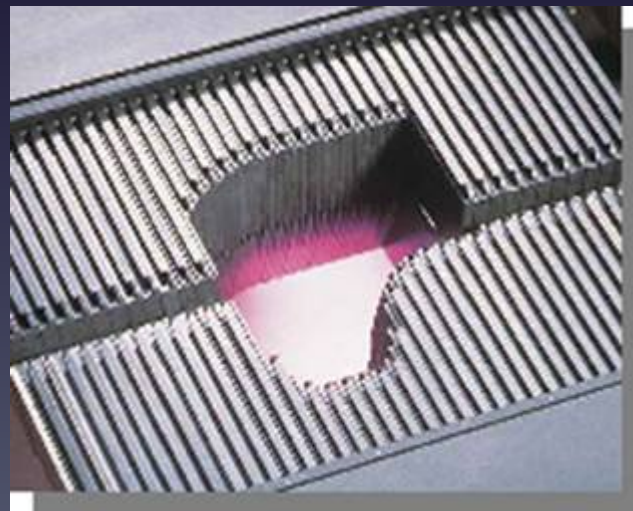




Dose volume histogram (DVH)



3. 模具製作或將參數輸入治療機



4. 治療病人



常用的放射劑量

- 術前同步放射化學治療
 - 45 格雷(Gy)/25 分次
 - 可考慮劑量加強到50 格雷(Gy)
- 根治性放射化學治療
 - 45~50 格雷(Gy)/25 分次
 - 可考慮劑量加強到55 格雷(Gy)
- 手術後照射
 - 45~54 格雷(Gy)/25~30分次
- 緩解性照射
 - 視狀況而定

治療時間

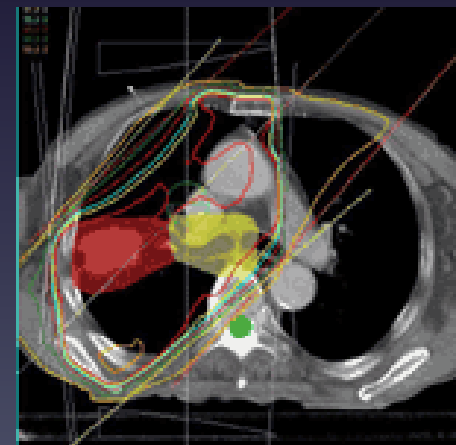
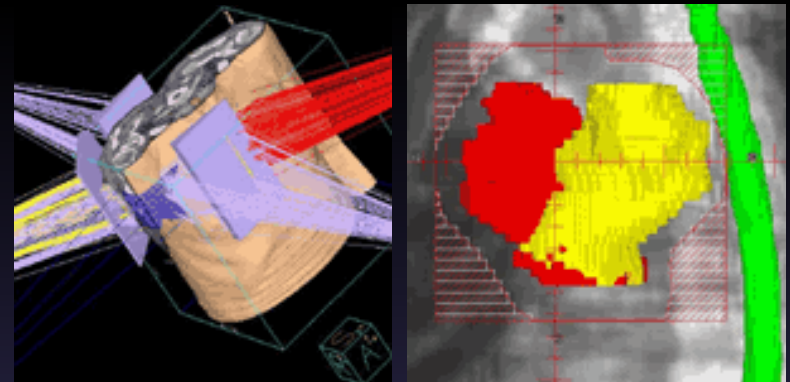
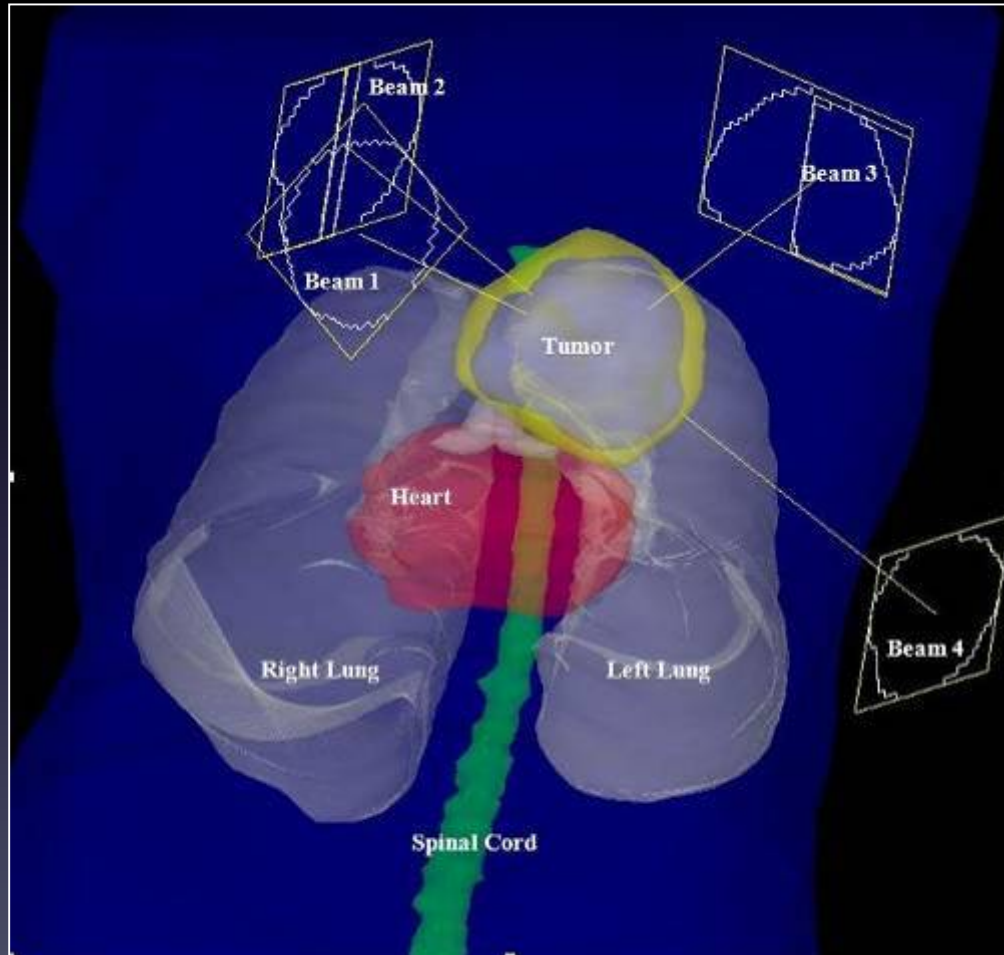
- 放射治療的時間是星期一到星期五，每天一次
- 每天在治療室中約十至十五分鐘，此時只有一人在治療室內，務必放鬆心情、靜躺不動且平和呼吸。
- 在這5-8週的時間，每週會有一次的例行門診，主治醫師會針對治療的副作用給予適當的治療。

放射治療的技術

放射治療技術

- Conventional (傳統治療)
- 3D Conformal Radiotherapy (三度空間順形治療)
- IMRT (強度調控治療)
- IGRT (影像導引治療)
- Tomotherapy (螺旋斷層放射治療，螺旋刀)
- VMAT (弧形調控放射治療)
- Stereotactic Radiosurgery (立體定位放射手術)

三度空間順形治療

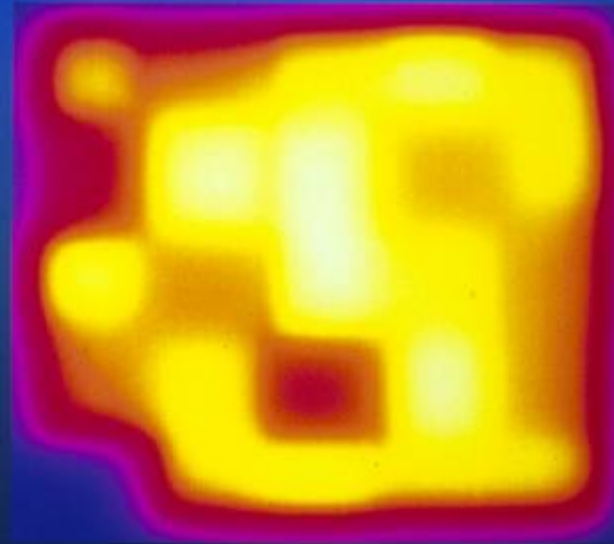


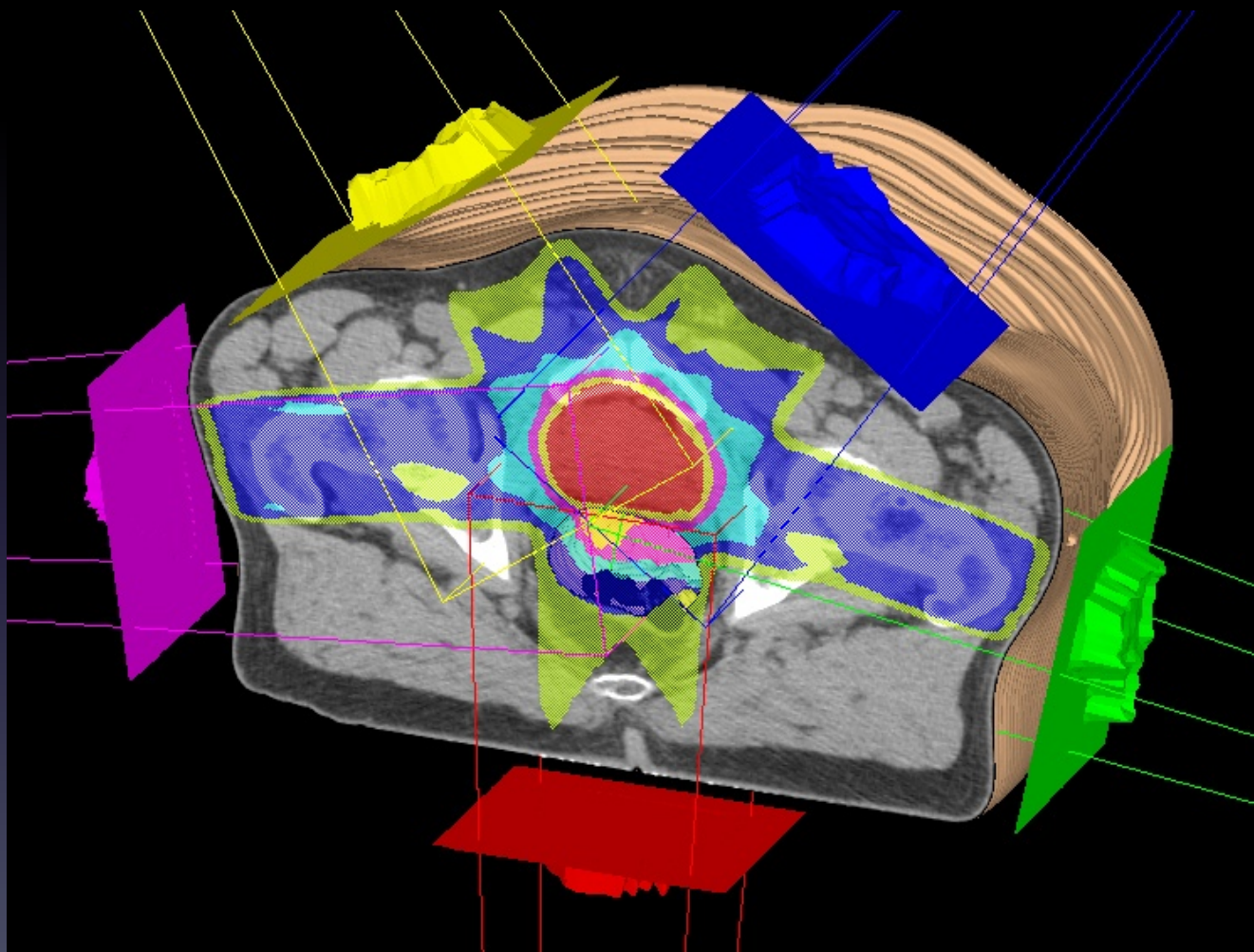
強度調控治療 (IMRT)

Conventional

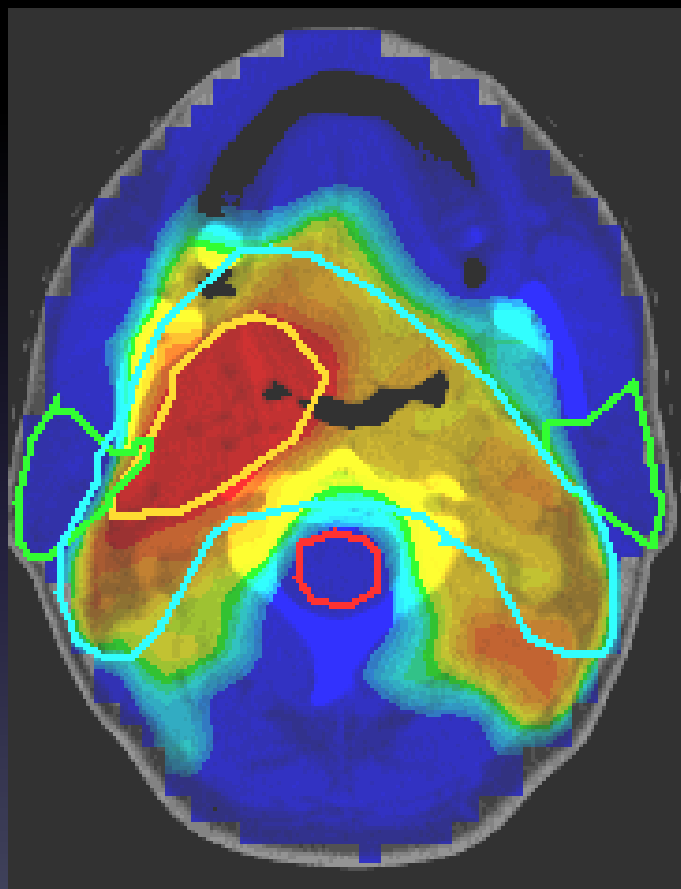


Intensity Modulated

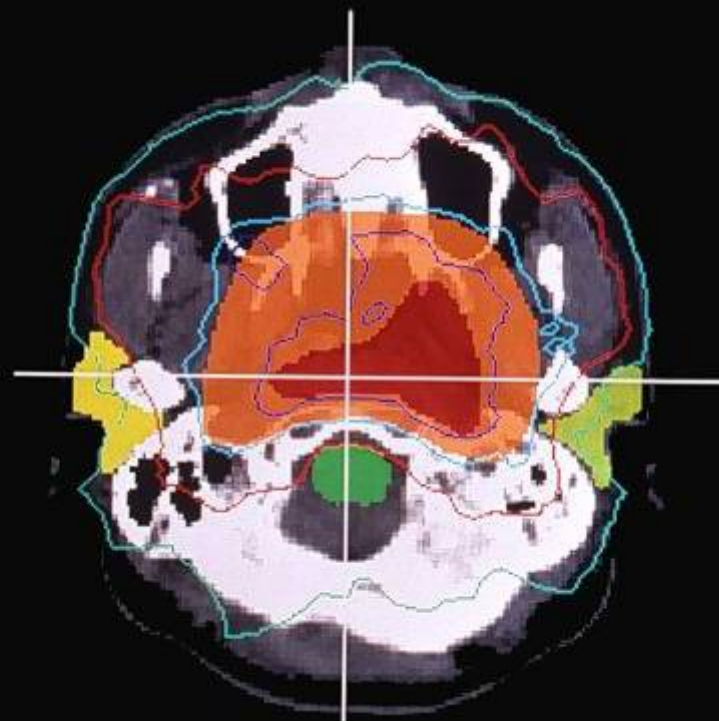




強度調控治療 (IMRT)



88%
75%
50%
30%

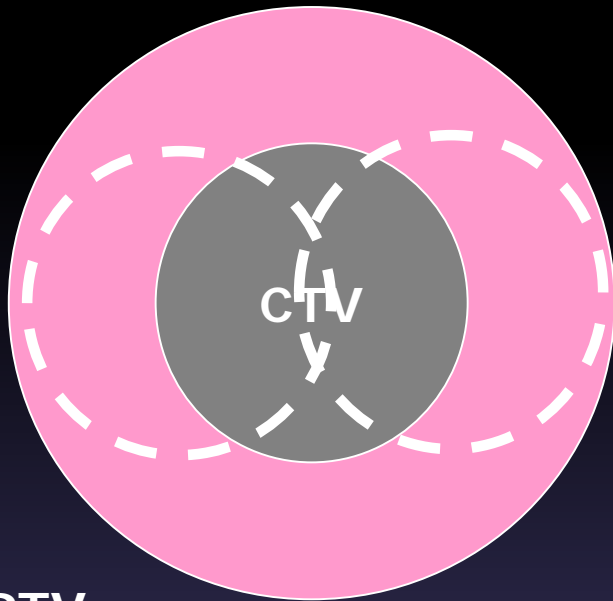


WT

IMRT v.s. 3DCRT

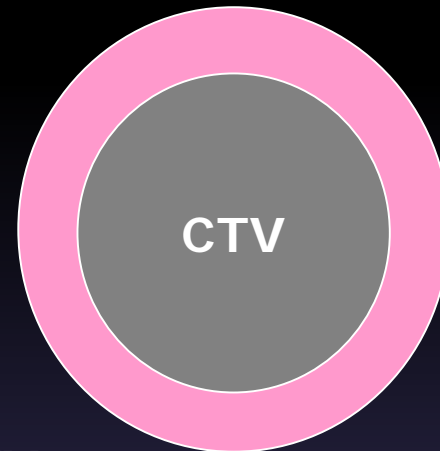
- 更好的放射劑量分布
 - 腫瘤包覆率
 - 重要器官保護
- 治療時間較長
- 需要更準確的定位

影像導引治療 (IGRT)



PTV

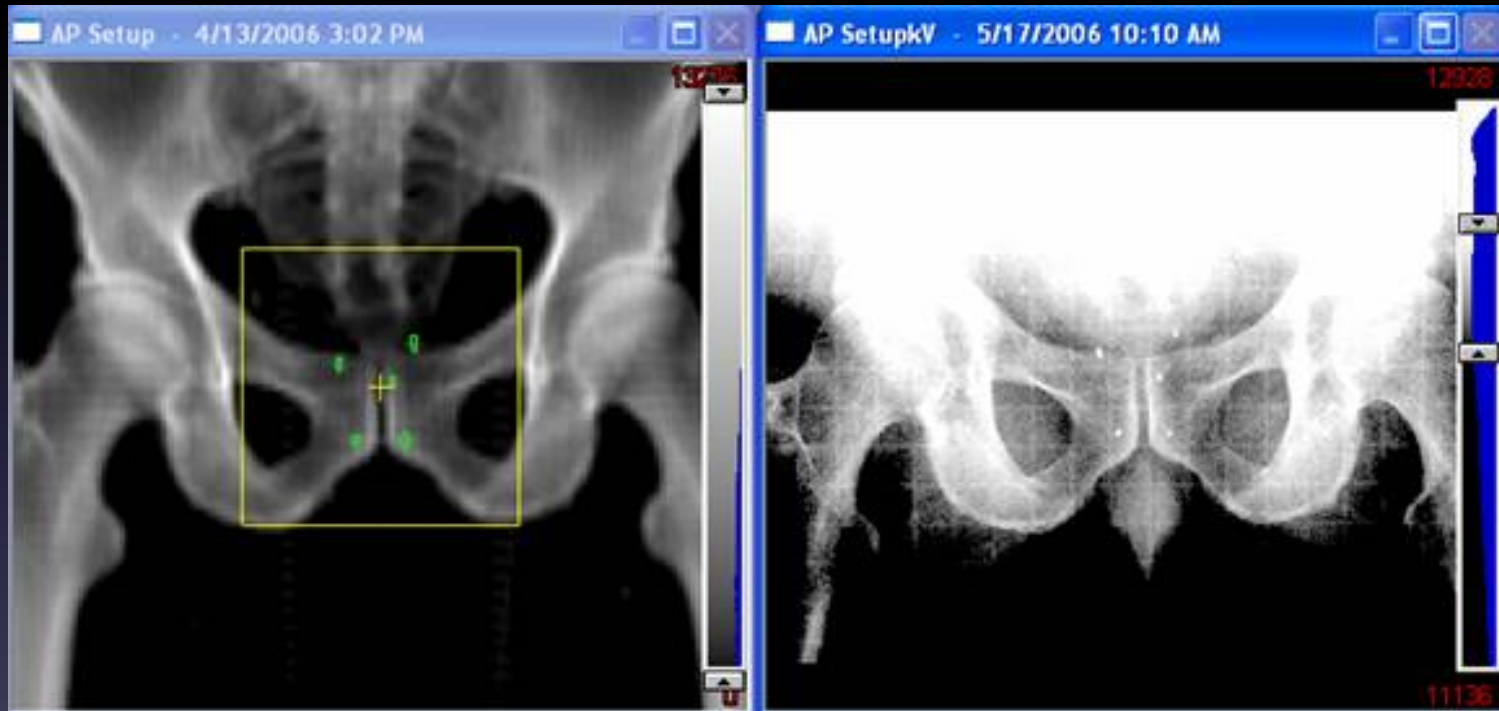
Without
Imaging



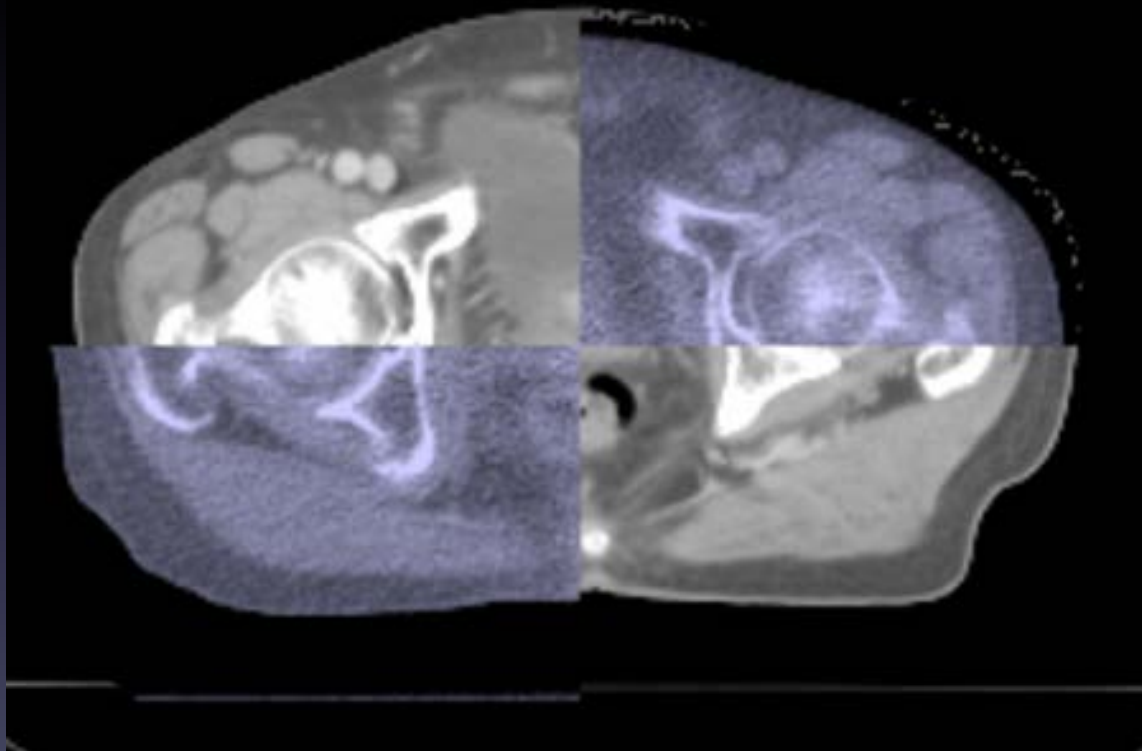
PTV

With
Imaging

驗證片

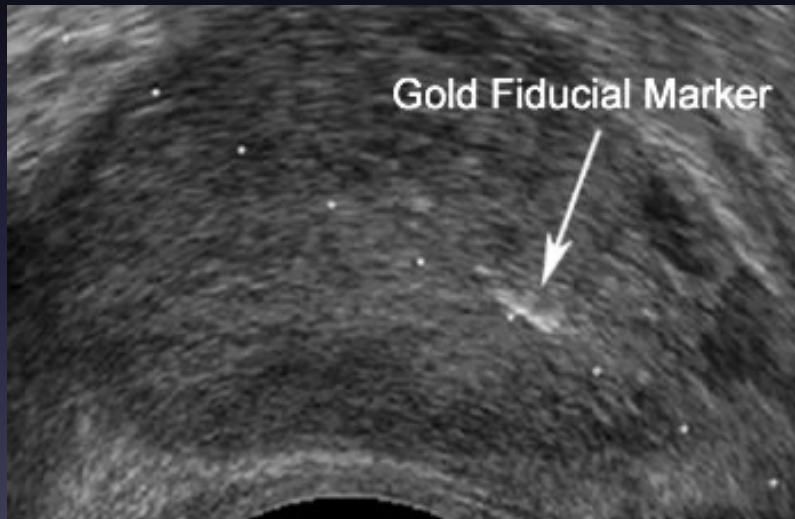


Cone beam CT



影像導引治療 (IGRT)

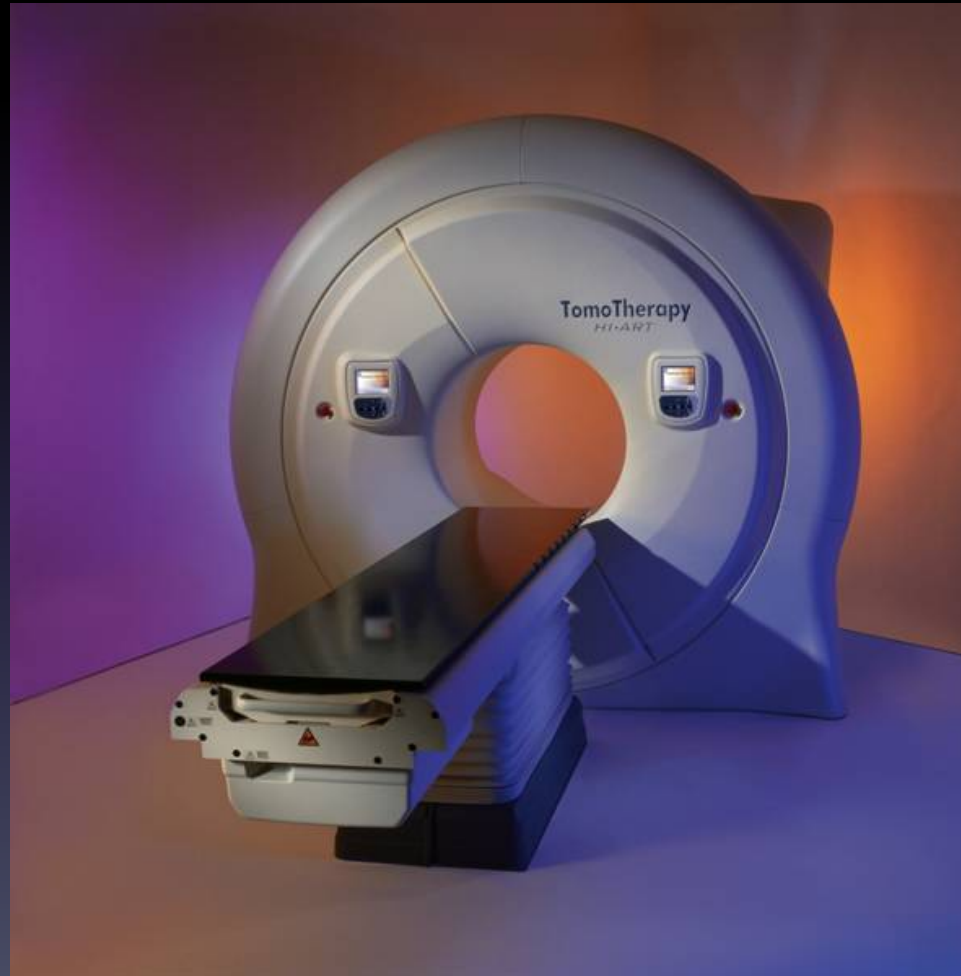
Markers attached to patient



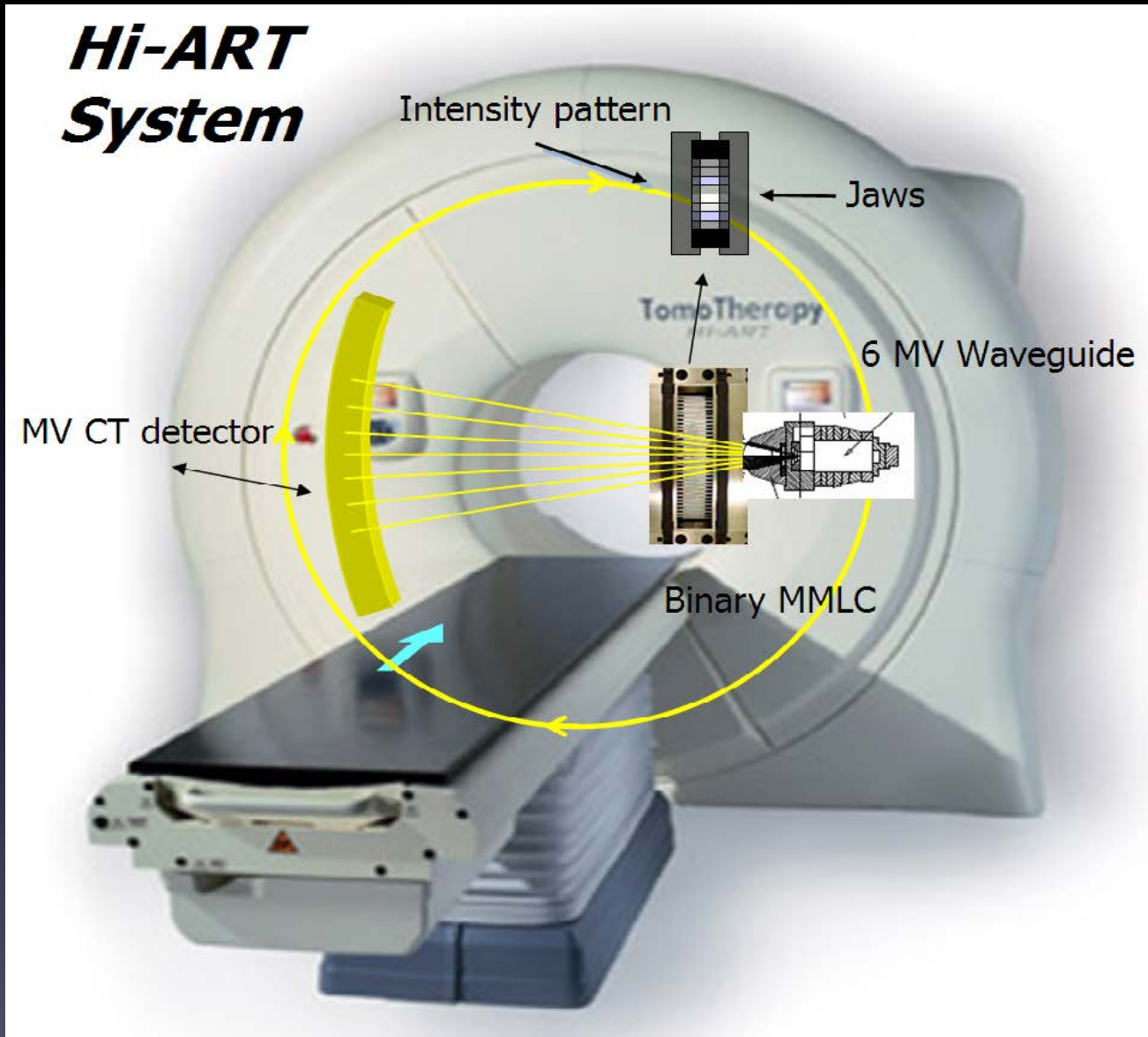
Prostate radiation external beam therapy includes Dr. Gheiler placing 4 tiny gold fiducial markers into the prostate so the radiation beam targets the prostate better.



螺旋斷層放射治療、螺旋刀 (Tomotherapy)



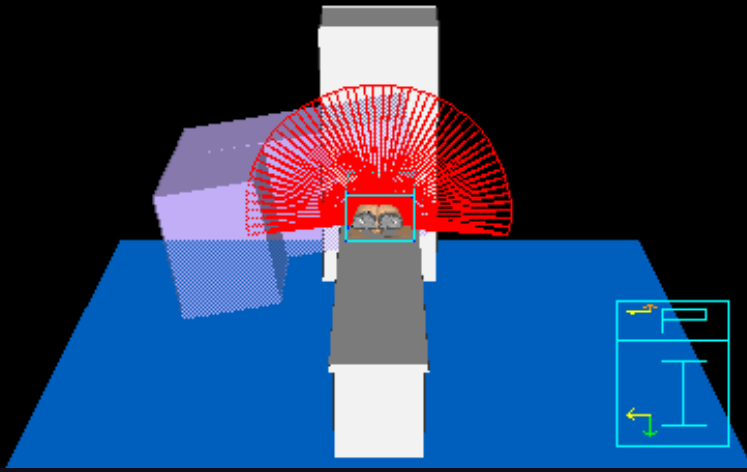
Basic structure of a Helical Tomotherapy Machine



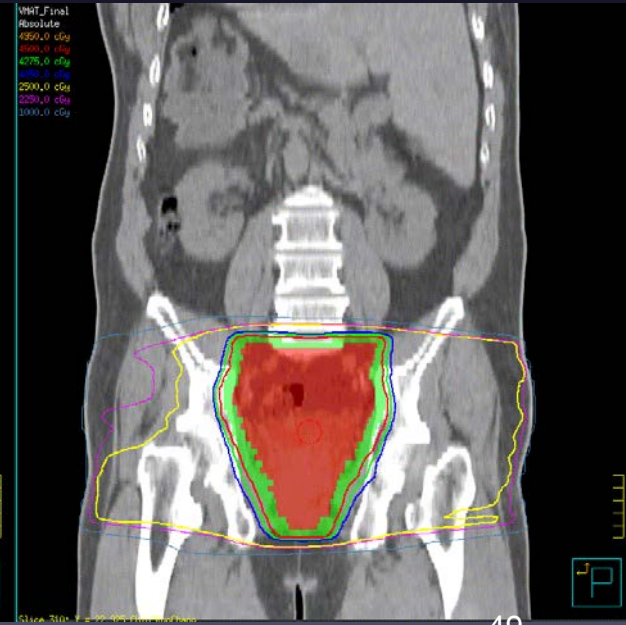
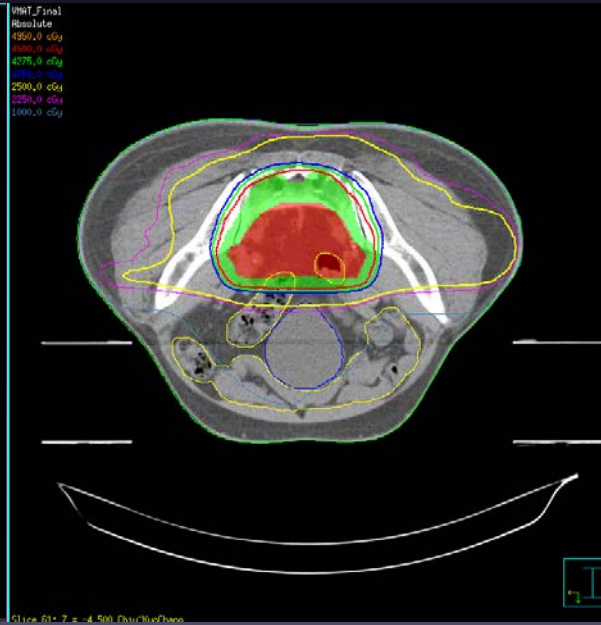
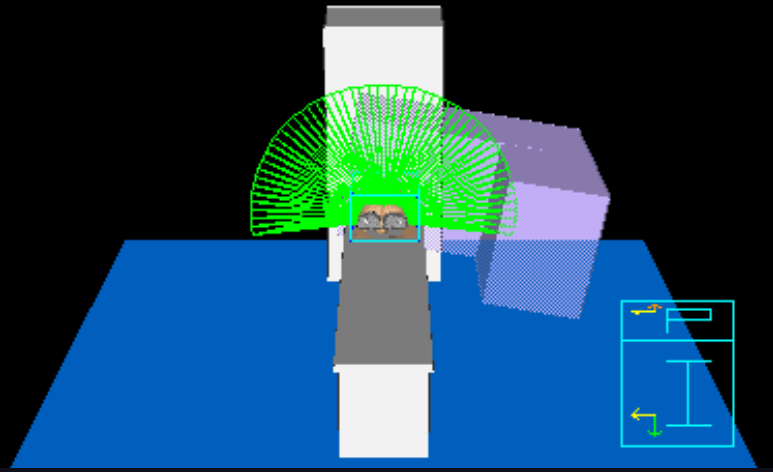
銳速刀、弧形刀 (Rapid Arc/VMAT)



VMAT_Final



VMAT_Final



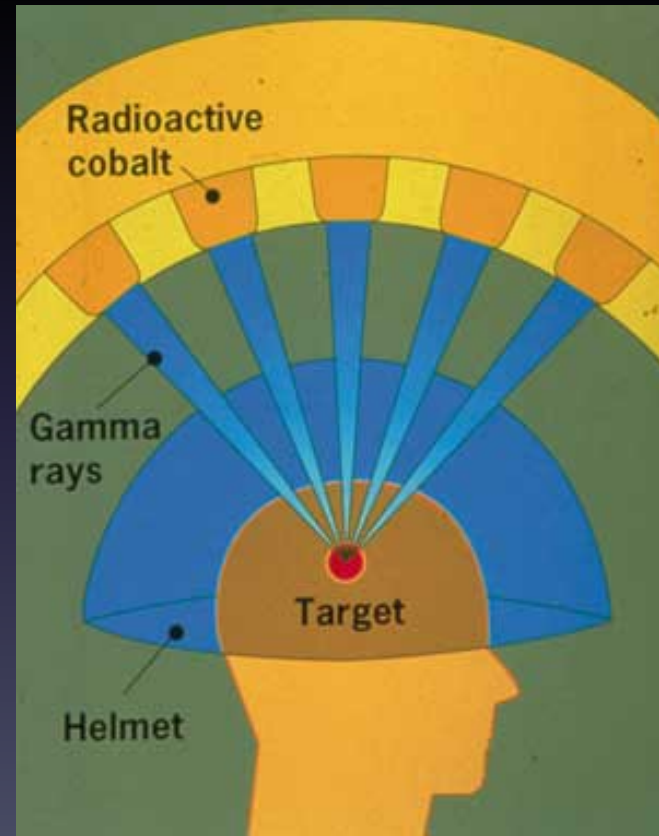
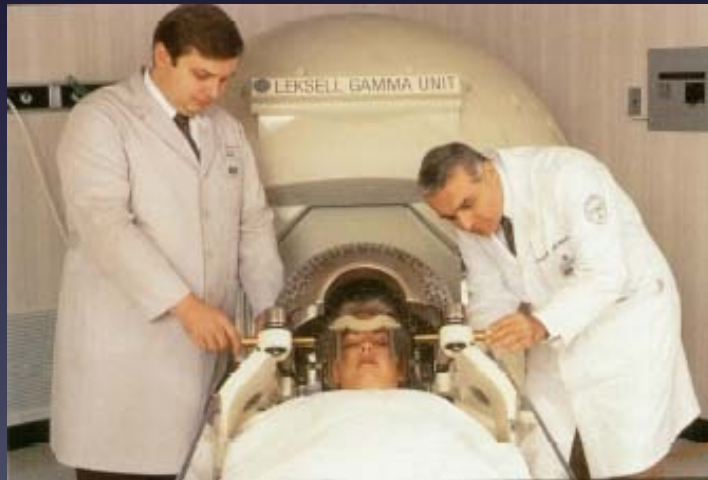
立體定位放射手術 (SRS)

- 以超高劑量的射線，經由幾百個角度，穿透組織，直接聚焦於腫瘤，殺死癌細胞
- 由於劑量很大，需配合非常精細的定位技術
- 早期用於腦部腫瘤
- 進一步用於全身其他腫瘤 → 立體定位放射治療 (SRT)

立體定位放射手術 (SRS)



Gamma knife



立體定位放射手術(SRS)



Cyberknife



放射治療的副作用

- 放射治療是局部治療，只會影響治療區域內細胞，治療時感覺就像照X光一樣，不會引起任何顯著熱量或電擊感，照射後在體內也不會有任何放射物質存在
- 急性反應：在大部分病人療程中隨劑量累積逐漸出現，但在療程結束後也一定會緩解
- 亞急性反應和慢性反應：療程結束後追蹤期才會出現，也僅發生在少數病人

急性反應

放射性皮膚炎

- 在放射治療約三到四星期後，在治療範圍內（包括前胸和後背）的皮膚會有紅、癢、色素沉著的反應。
- 避免用肥皂清洗或磨擦，只能用溫清水輕輕洗過，以柔軟毛巾輕輕拍乾而不是擦乾。
- 在療程結束一到二週後方可使用肥皂。

放射性腸炎

- 在治療約二到三星期後，因腸道受到照射，可能會有腸道蠕動加快甚至有腹瀉的狀況。
- 在這段期間飲食宜避免刺激腸道活動的食物。
- 這現象於放射治療結束後，約一至二週會慢慢消失。

疲倦感

- 在接受放射治療的期間常會變得較疲倦，尤其在治療的最後幾週，一般在療程結束後會逐漸恢復。

亞急性反應

放射治療後手術併發症

- 少數病人因放射治療前後進行手術，產生傷口癒合不良、壞死、或是腸道滲漏、形成瘻管。

慢性反應

放射性纖維化

- 可能會導致被照射的組織纖維化，於治療結束後幾個月發生
- 纖維化很像結疤，多數病人因纖維化程度不高不會有任何症狀，但若之後要再進行手術可能會影響手術之進行。

慢性放射性腸炎

- 因放射線造成的腸道黏膜破損
- 可能有出血、壞死現象

放射治療的效果

膽管癌

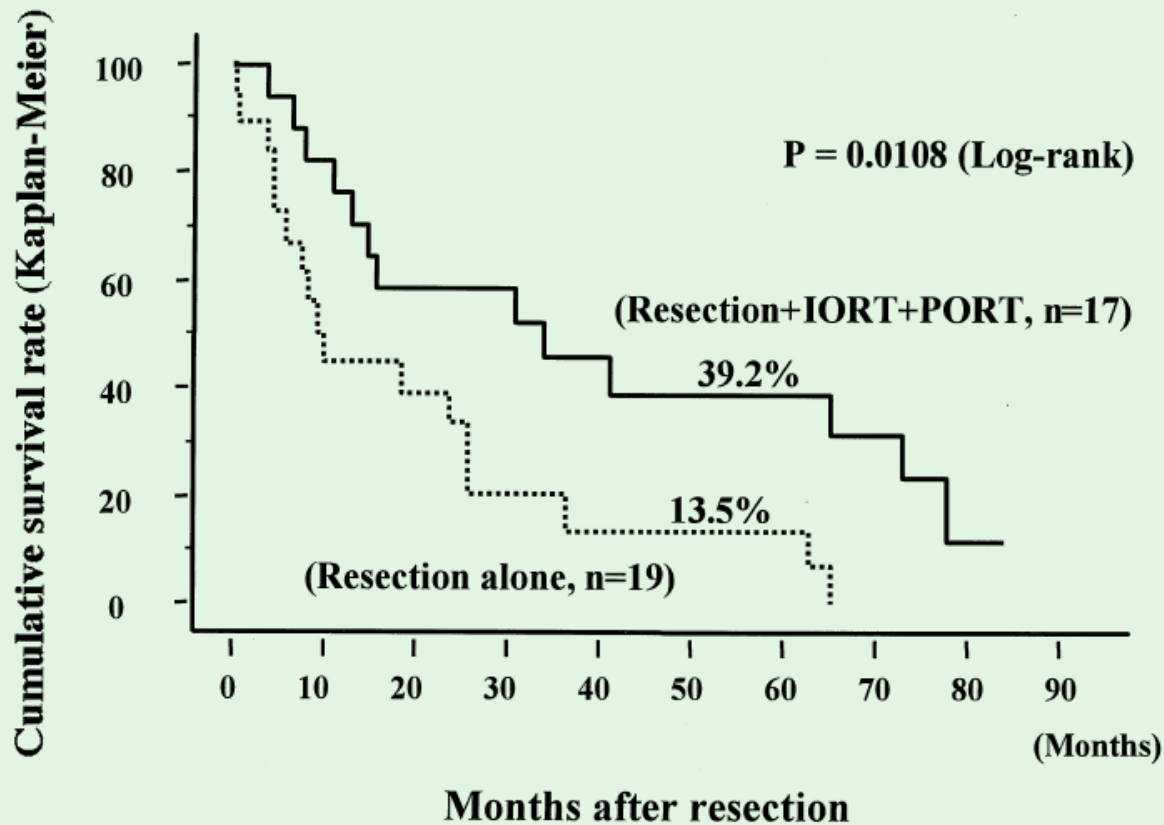


Fig. 2. Survival curves of patients with Stage IVA disease after resection, followed by adjuvant radiotherapy of microscopic residue (RT1) with IORT plus PORT.

緩解性照射

- 改善疼痛
- 緩解膽道阻塞

胰臟癌

TABLE 59.4 PROSPECTIVE, RANDOMIZED TRIALS FOR ADJUVANT THERAPY FOR PANCREATIC CANCER

<i>Series (Reference)</i>	<i>Number of Patients</i>	<i>Median Survival (Month)</i>	<i>2-Year Survival (%)</i>	<i>5-Year Survival (%)</i>
GITSG (73)				
Chemoradiation	21	20.0	42	15
Observation	22	10.9	15	5
Chemoradiation (expanded cohort) (74)	30	18.0	46	17
EORTC (75,76)				
Chemoradiation	110	21.6	51	25
Observation	108	19.2	41	22
ESPAC-1 Pooled Data (78)				
Chemotherapy	238	19.7	NA	NA
No chemotherapy	235	14.0	NA	NA
Chemoradiation	175	15.5	NA	NA
No chemoradiation	178	16.1	NA	NA
ESPAC-1 2x2 analysis (79)				
Chemotherapy	147	20.1	40	21
No chemotherapy	142	15.5	30	8
Chemoradiation	145	15.9	29	10
No chemoradiation	144	17.9	41	20
CONKO (80,81)				
Chemotherapy (gemcitabine)	186	23	30.5	21
Observation	182	20	14.5	9
ESPAC-3 (83)				
Chemotherapy (5-FU)	551	23	48	NA
Chemotherapy (gemcitabine)	537	23.6	49	NA
RTOG-9704 (Pancreatic Head) (84–86)				
Gemcitabine then chemoradiation	187	20.5	31 (3 year)	22
5-FU then chemoradiation	201	17.2	22 (3 year)	18

EORTC, European Organisation for Research and Treatment of Cancer; ESPAC, European Study Group for Pancreatic Cancer; GITSG, Gastrointestinal Tumor Study Group; NA, not available; CONKO, Charite Onkologie; 5-FU, 5-fluorouracil; RTOG, Radiation Therapy Oncology Group.

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TABLE 59.5 PROSPECTIVE RANDOMIZED TRIALS FOR LOCALLY ADVANCED, UNRESECTABLE PANCREATIC CANCER

<i>Series (Reference)</i>	<i>Number of Patients</i>	<i>Median Survival (Month)</i>	<i>Local Failure (%)</i>	<i>1-Year (%)</i>	<i>18-Month (est %)</i>
EBRT Versus CRT					
Mayo Clinic (111)					
EBRT (35–40 Gy/3–4 weeks) alone	32	6.3	NA	6	6
EBRT (35–40 Gy/3–4 weeks) + 5-FU	32	10.4	NA	22	13
GITSG (112)					
EBRT (60 Gy/10 weeks) alone	25	5.3	24	10	5
EBRT (40 Gy/6 weeks) + 5-FU	83	9.7	26	35	20
EBRT (60 Gy/10 weeks) + 5-FU	86	9.3	27	46	20
ECOG (113)					
EBRT (59.4 Gy) alone	49	7.1	NA	NA	NA
EBRT (59.5 Gy) + 5-FU/MMC	55	8.4	NA	NA	NA
Variations in CRT Regimen					
GITSG (114)					
EBRT (60 Gy/10 weeks) + 5-FU	73	8.5	58 (first site)	33	15
EBRT (40 Gy/4 weeks) + doxorubicin	70	7.6	51 (first site)	27	17
Taipei (115)					
EBRT (50.4–61.2 Gy) + 5-FU	16	6.7	56	31	0 (2 year)
EBRT (50.4–61.2 Gy) + Gemcitabine	18	14.5	34	56	15 (2 year)
CRT Versus Chemotherapy					
GITSG (116,159)					
EBRT (54 Gy/6 weeks) + 5-FU and SMF	22	9.7	45 (first site)	41	18
SMF alone	21	7.4	48 (first site)	19	0
ECOG (117)					
EBRT (40 Gy/4 weeks) + 5-FU	47	8.3	32	26	11
5-FU alone	44	8.2	32	32	21
FFCD/SFRO (118)					
EBRT (60 Gy) + 5-FU/CDDP	59	8.6	NA	32	NA
Gemcitabine alone	60	13	NA	53	NA
ECOG (119)					
EBRT (50.4 Gy) + Gemcitabine	34	11.1	12 (first site)	50	29
Gemcitabine alone	37	9.2	30 (first site)	32	11

EBRT, external beam radiation therapy; CRT, chemoradiation; NA, not available; 5-FU, 5-fluorouracil; CDDP, neoadjuvant cisplatin; GITSG, Gastrointestinal Tumor Study Group; ECOG, Eastern Cooperative Oncology Group; MMC, mitomycin-C; SMF, streptozocin, mitomycin-C, and 5-fluorouracil; FFCD/SFRO, Fédération Francophone de Cancérologie Digestive/Société Francophone de Radiothérapie Oncologique.

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總結

- 放射治療為分次治療，週一至週五每日治療約15~20分鐘，週六日休息。
- 在膽管癌，適應症主要為術後有微觀殘留腫瘤，或是無法手術的狀況。
- 在胰臟癌，適應症主要為術後有微觀殘留腫瘤、無法手術的狀況，或是嘗試將無法手術狀況變為可手術。
- 副作用主要為疲倦、腹瀉以及少數病人產生腸道受傷。