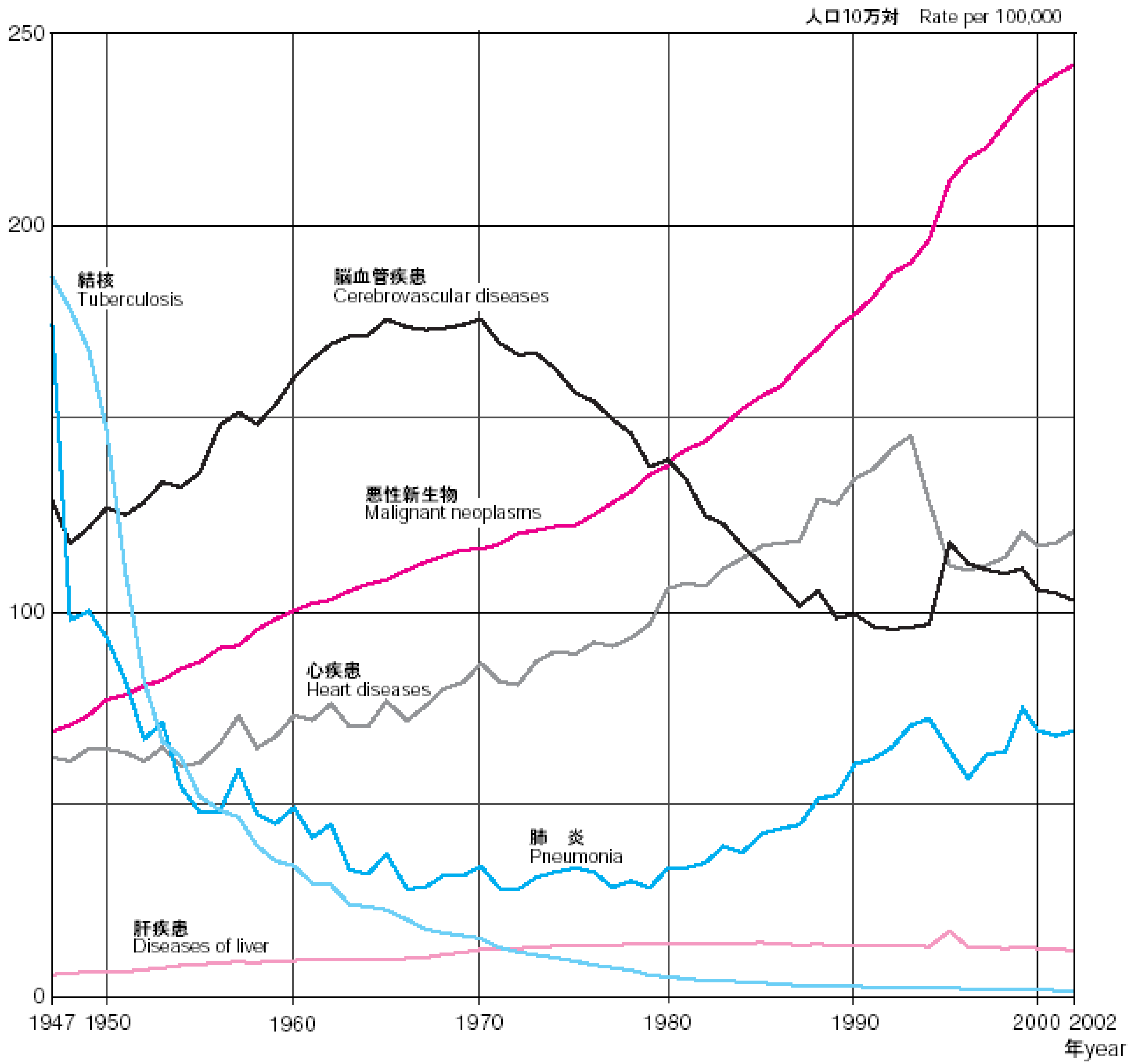
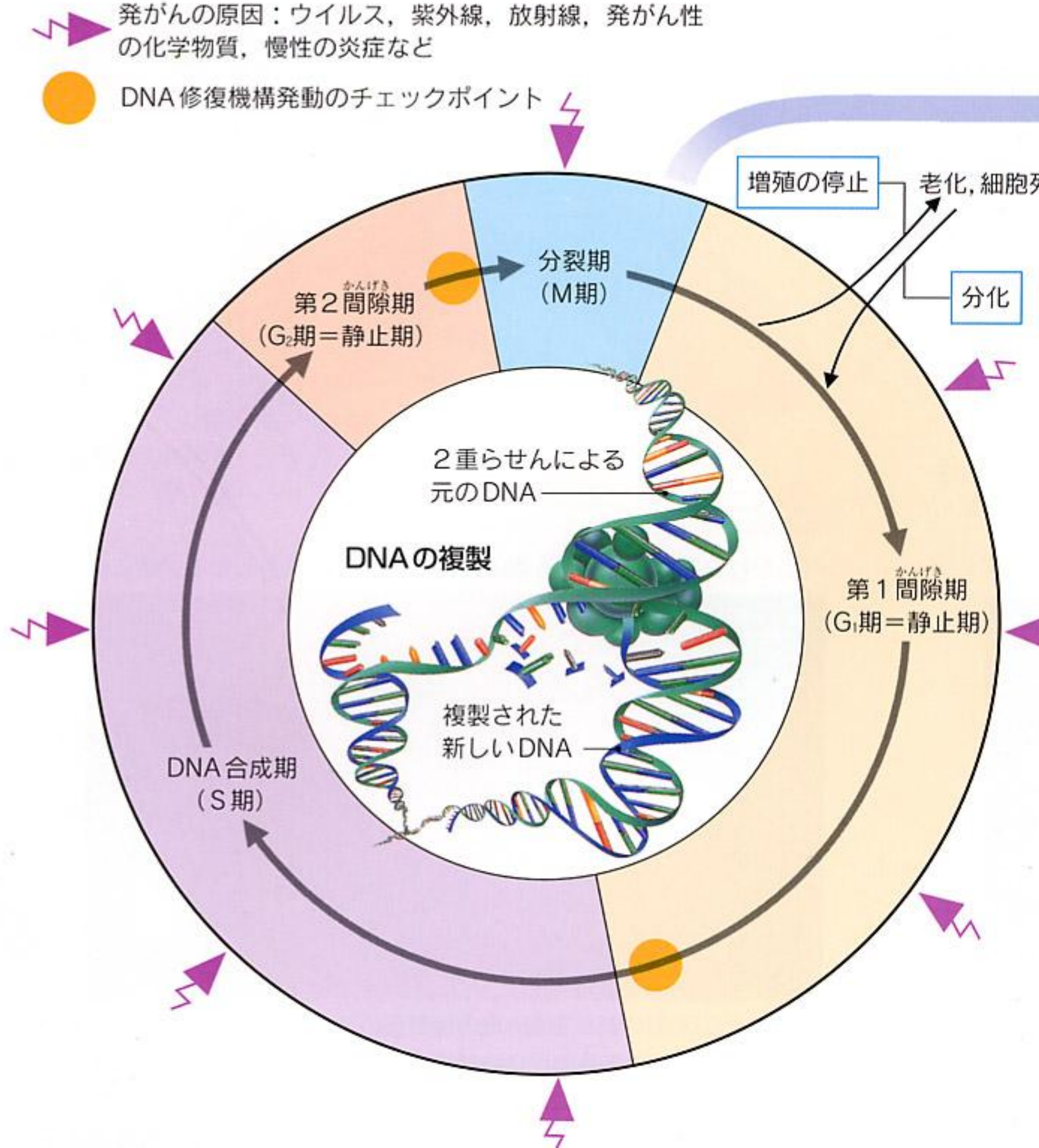
切らずに治すがん治療

科学カフェー
2009．5．16．

1 死亡率の推移（昭和22年～平成14年）
Annual mortality trends for leading causes of death in Japan (1947～2002)

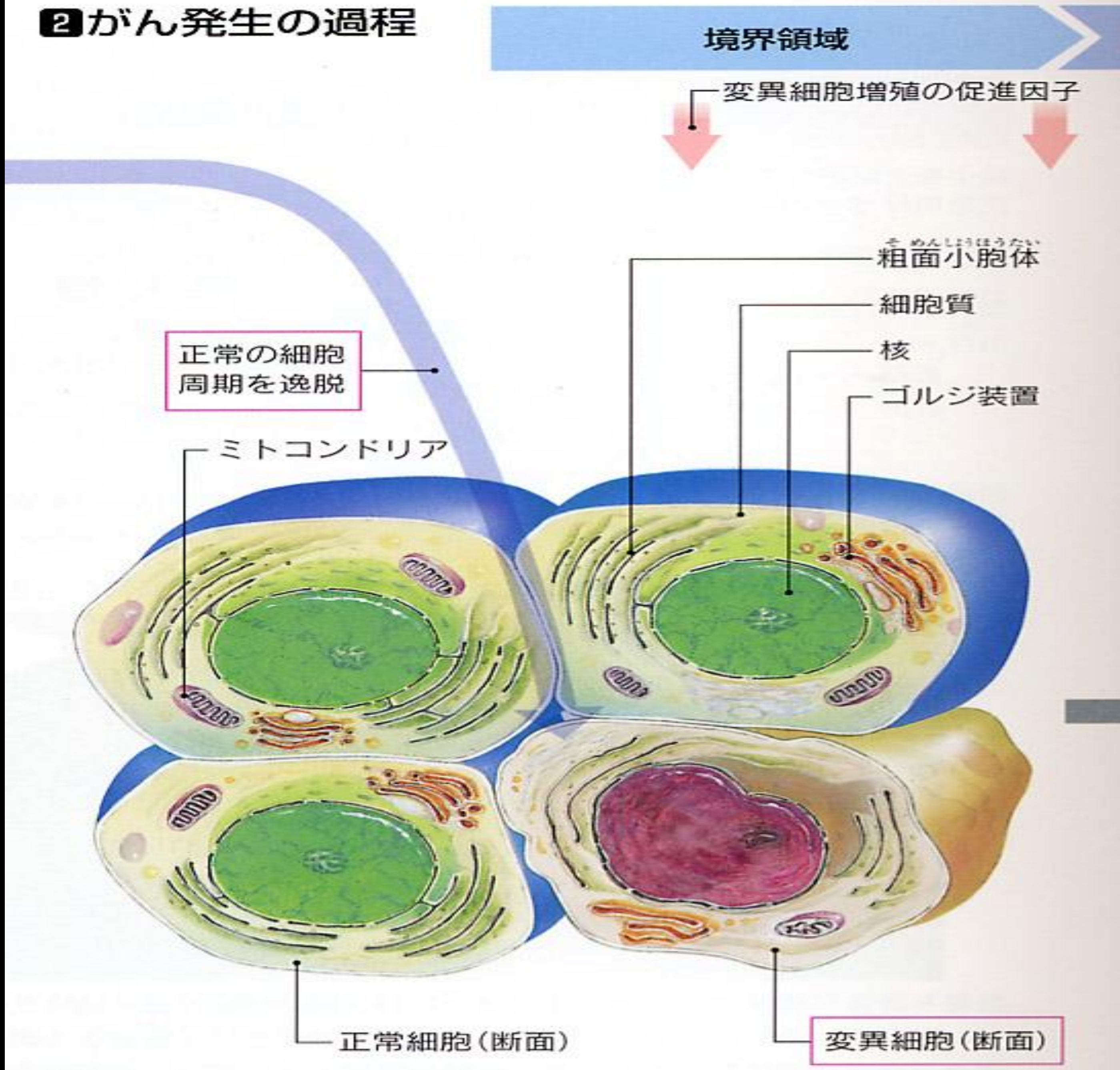


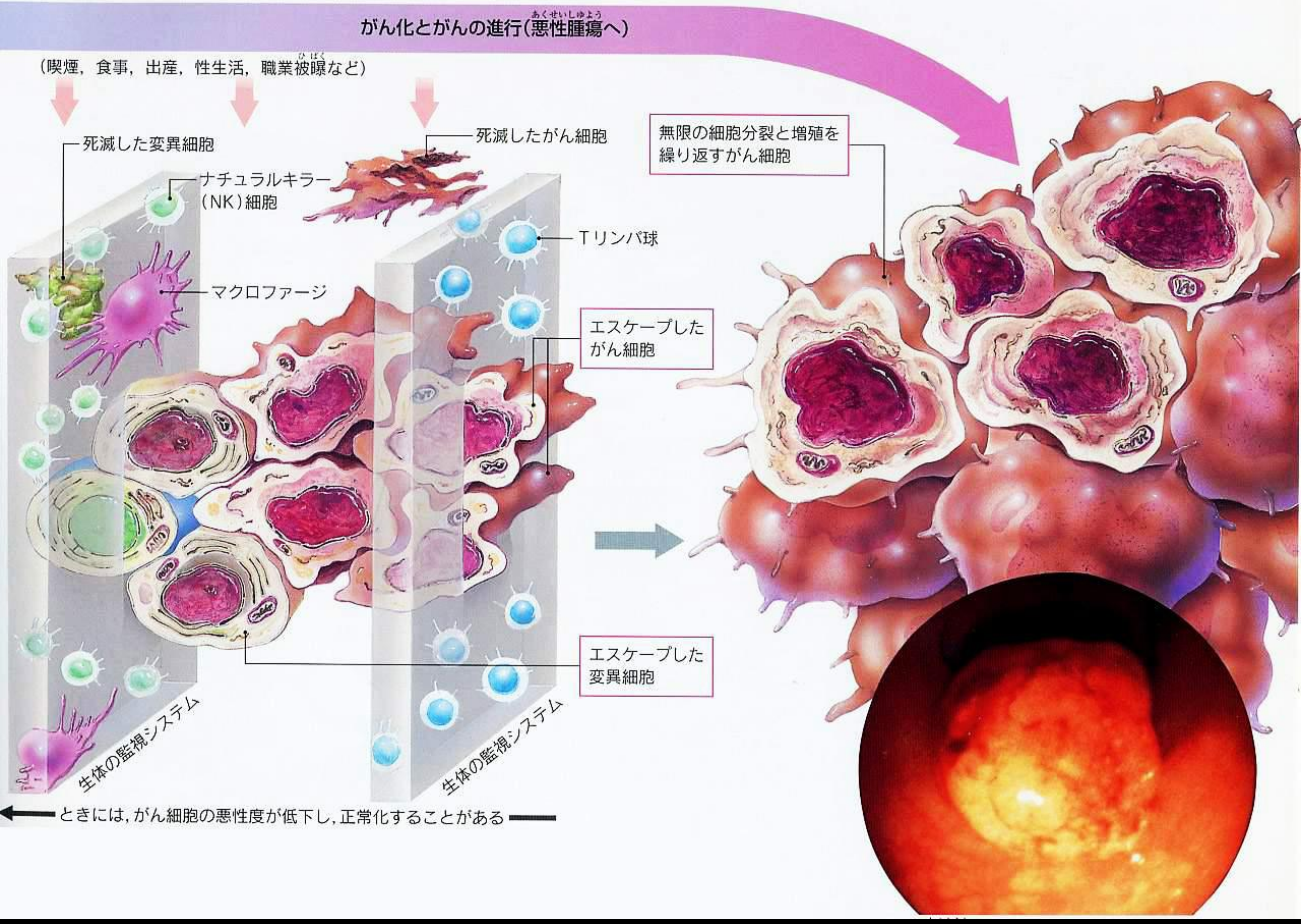
❶細胞周期と細胞分裂



発がんの原因：ウイルス，紫外線，放射線，発がん性の化学物質，慢性の炎症など
DNA 修復機構発動のチェックポイント
増殖の停止
老化，細胞死
分化
分裂期
（M期）
第2間隙期
（G₂期＝静止期）
第1間隙期
（G₁期＝静止期）
DNA合成期
（S期）
2重らせんによる
元のDNA
DNAの複製
複製された
新しいDNA

❷がん発生の過程


境界領域
変異細胞増殖の促進因子
粗面小胞体
そめんしょうほうたい
細胞質
核
ゴルジ装置
正常の細胞
周期を逸脱
ミトコンドリア
正常細胞（断面）
変異細胞（断面）


がん化とがんの進行（悪性腫瘍へ）
（喫煙，食事，出産，性生活，職業被曝など）
死滅した変異細胞
ナチュラルキラー（NK）細胞
マクロファージ
死滅したがん細胞
Tリンパ球
エスケープしたがん細胞
エスケープした変異細胞
無限の細胞分裂と増殖を繰り返すがん細胞
生体の監視システム
生体の監視システム
ときには，がん細胞の悪性度が低下し，正常化することがある

がん治療の種類

外科治療 ─┐
　　　　　├─ 局所療法
放射線治療 ─┘

抗がん剤治療 ── 全身療法

免疫療法

温熱療法

放射線治療の歴史と進歩

W. C. Röntgen.

nahme zur Zeit von Röntgens Entdeckung, die uns damals von Röntgen geschenkt wurde.

Ueber eine neue Art von Strahlen

von W. C. Röntgen

(Vorläufige Mittheilung)

1. Lässt man durch eine Hittorf'sche Vacuumröhre, oder einen genügend evacuirten Lenard'schen, Crookes'schen oder ähnlichen Apparat die Entladungen eines grösseren Ruhmkorff's gehen und bedeckt ~~den [illegible] Apparat~~ die Röhre mit einem ziemlich eng anliegenden Mantel aus dünnem schwarzem Carton, so sieht man in dem vollständig verdunkelten Zimmer einen in die Nähe des Apparates gebrachten, mit Bariumplatincyanür angestrichenen Papierschirm bei jeder Entladung hell aufleuchten, fluoresciren, gleichgültig ob die angestrichene oder die andere Seite des Schirmes dem Entladungsapparat zugewendet ist. Die Fluorescenz ist noch in 2 m Entfernung vom Apparat bemerkbar.

Man überzeugt sich leicht, dass die Ursache der Fluorescenz vom Innern des Entladungsapparates und von keiner anderen Stelle der Leitung ausgeht.

EINE NEUE ART

VON

STRAHLEN.

VON

DR. W. RÖNTGEN,

O. Ö. PROFESSOR AN DER K. UNIVERSITÄT WÜRZBURG

WÜRZBURG.

VERLAG UND DRUCK DER STAHEL'SCHEN K. HOF- UND UNIVERSITÄTS-

BUCH- UND KUNSTHANDLUNG.

Ende 1895.

60 ₰.

KONGLIGA SVENSKA VETENSKAPS-AKADEMIEN

har vid sitt sammanträde den 12 Nov. 1901 i enlighet med föreskrifterna i det af

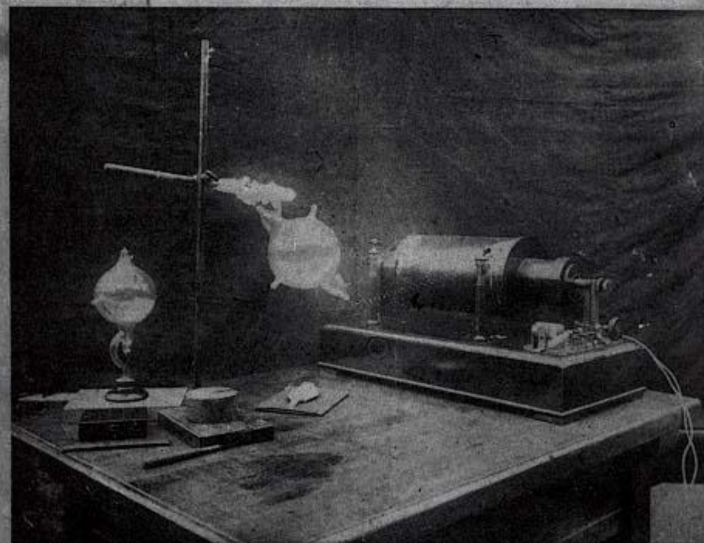
ALFRED NOBEL

den 27 November 1895 upprättade testamente beslutat att tilldela det pris som detta år bortgifves åt den som inom fysikens område har gjort den viktigaste upptäckt eller uppfinning till

WILHELM CONRAD RÖNTGEN

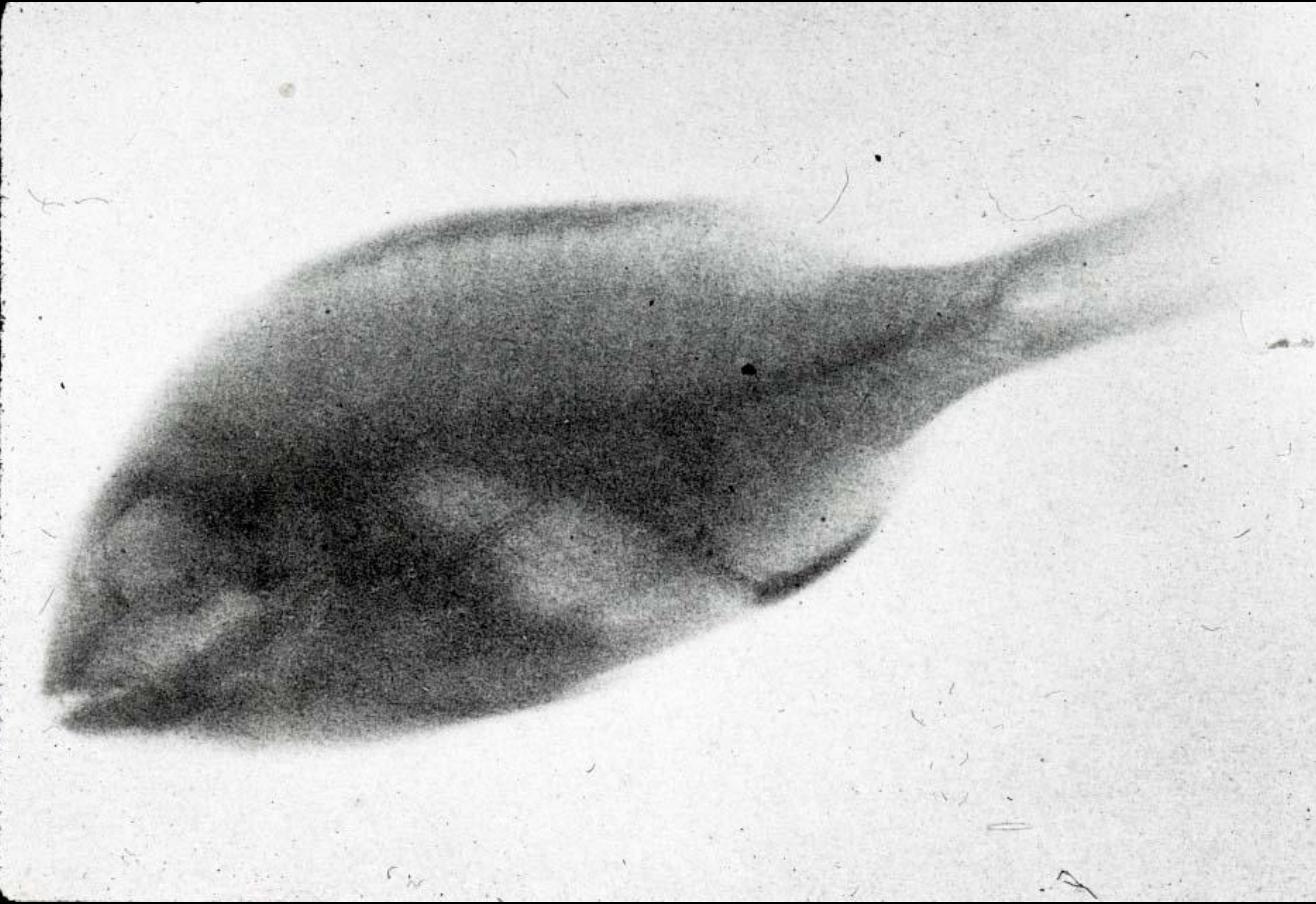
såsom ett erkännande af den utomordentliga förtjenst han inlagt genom upptäckten

れんとげん投影寫眞帖



第一高等學校

藏版



...tion of *Mus musculus* is greatly affected by strong sun- ...ven when all heat-rays have been screened off; and the ... the same for rays from all parts of the spectrum. ...ificial lights, such as the electric light or incandescent ... like sunshine when concentrated on the animals, but ...o effect when merely used to light a room. (4) The light ...eissler's tubes has no effect. (5) Röntgen rays have no ...on the quantity of CO_2 eliminated from the animal, what- ... the condition of the latter; that is, whether fasting or after ... whether previously kept for several hours in darkness, ... *versâ*. (6) What was observed with each of the six ...experimented on was strong excitement, which continued ...veral hours after the experiments with Röntgen rays had ... The moles, after being exposed to Röntgen rays for ...our, ran about in a nervous and excited way, and would ... (7) This excitement Prof. Capranica attributes to the ...cal effects of the Röntgen rays. (8) Experiments on cold- ...ed animals (*Coronella*) give, as yet, no appreciable results.

...e meteorological and astronomical work accomplished ...g 1895 in the Observatory of the Mersey Docks and Harbour ..., are stated by Mr. W. E. Plummer in a report just ...ed. Appended to the general tables is a catalogue and discussion of all the gales of wind that have been auto- ...ally recorded with velocities equal to, or exceeding, fifty ...per hour. Several interesting points are brought out by ...atalogue. It appears that the average length of a storm at ...pool, as defined by the condition that the wind velocity exceed fifty miles per hour, is about six hours; while the ...e number of stormy hours in a year does not greatly ...d sixty. With regard to the time of year in which these ...bances occur, general experience points to a connection ...en them and the observed temperature. This agreement ...y clearly shown by Mr. Plummer in a diagram having a

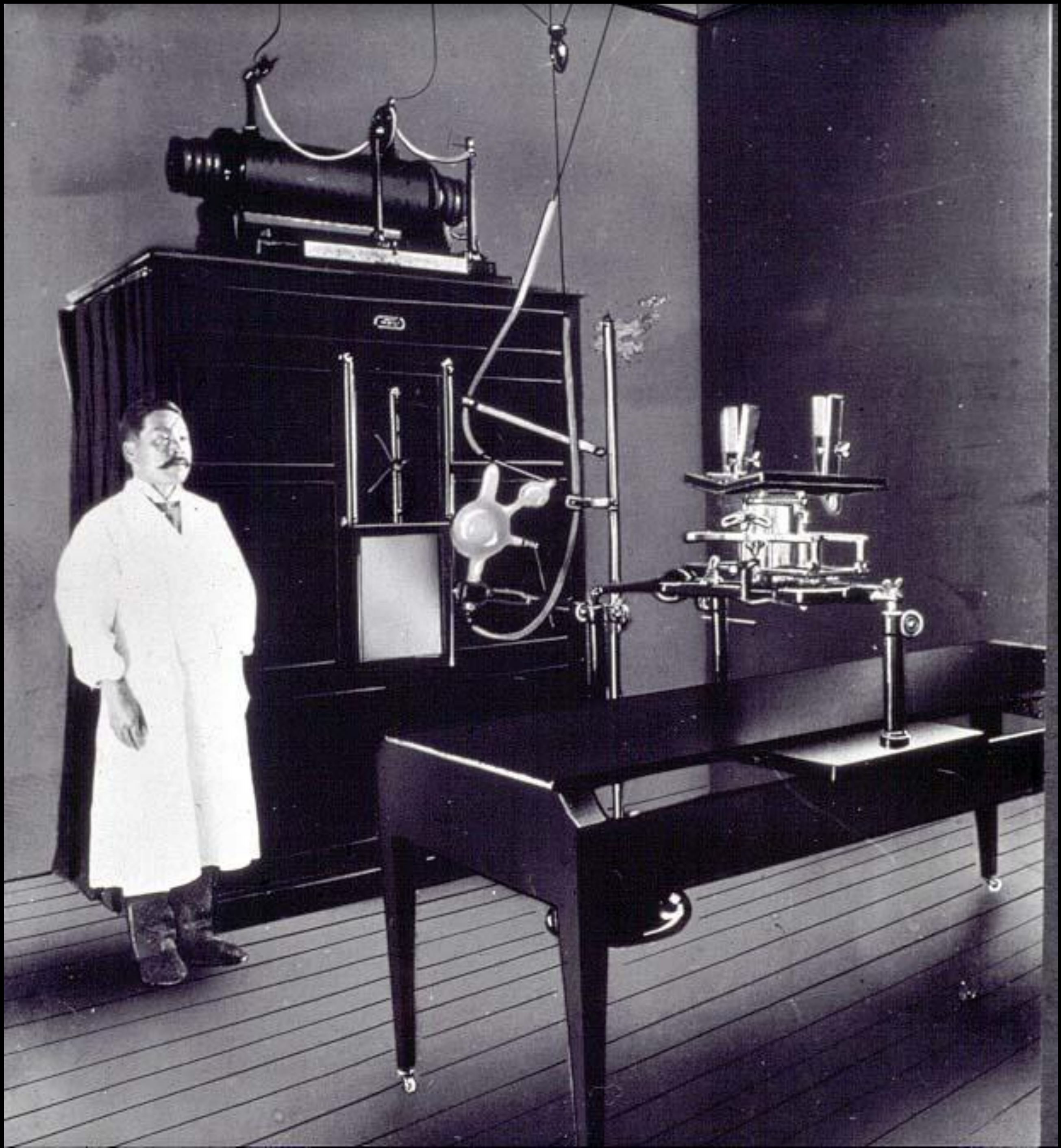
literature, new maps, and illustrations, it is an invaluable publication to geographers.

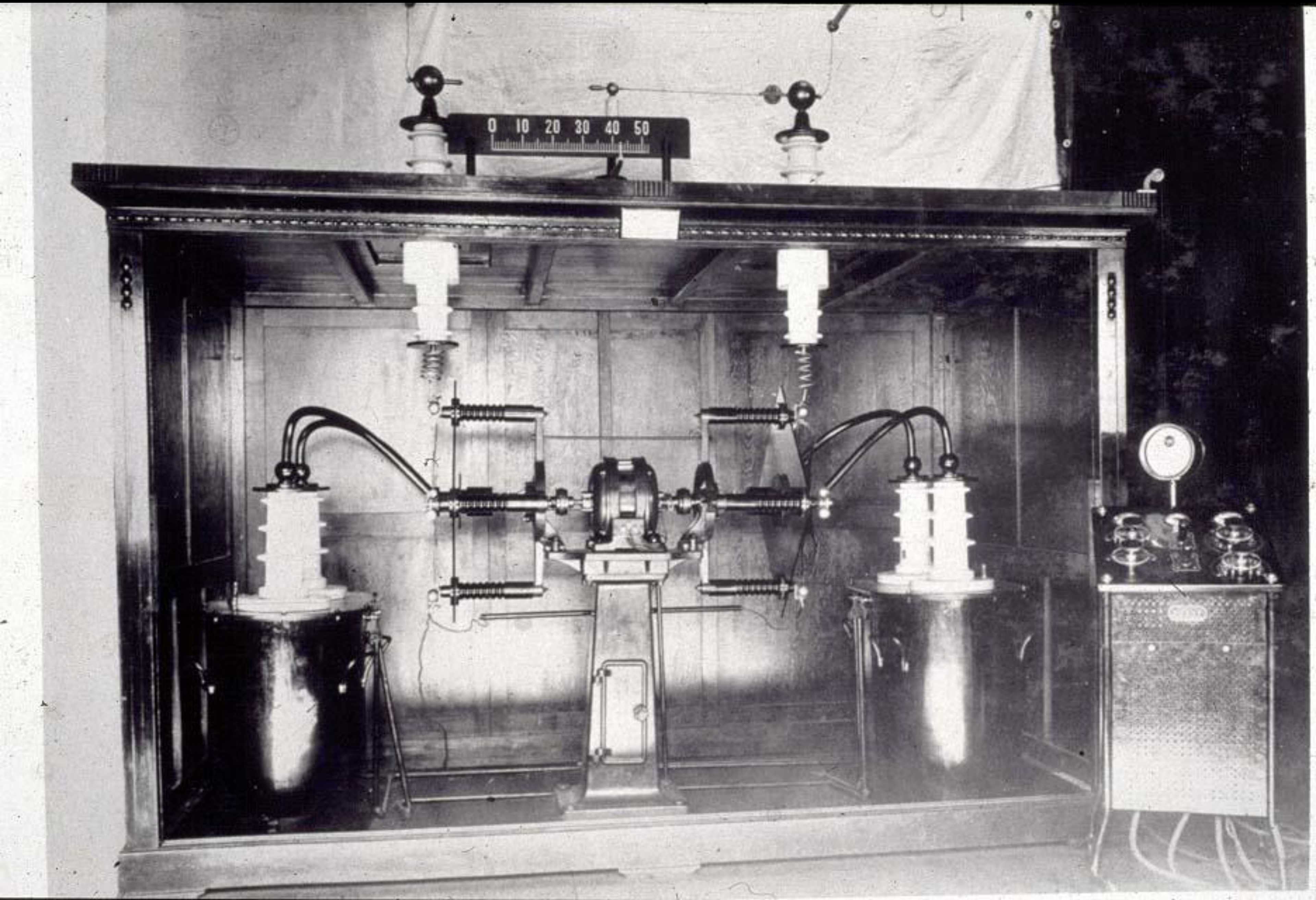
A SERIES of sixteen reproductions of photographs obtained by means of Röntgen rays, together with text (in Japanese) explanatory of the methods by which they were obtained, has been received from Prof. Y. Yamaguchi and T. Mizuno, of Tōkiō University. The photographs are much less distinct than those obtained since the introduction of the focus tube, but they nevertheless show that Japan means to keep in the van of scientific progress.

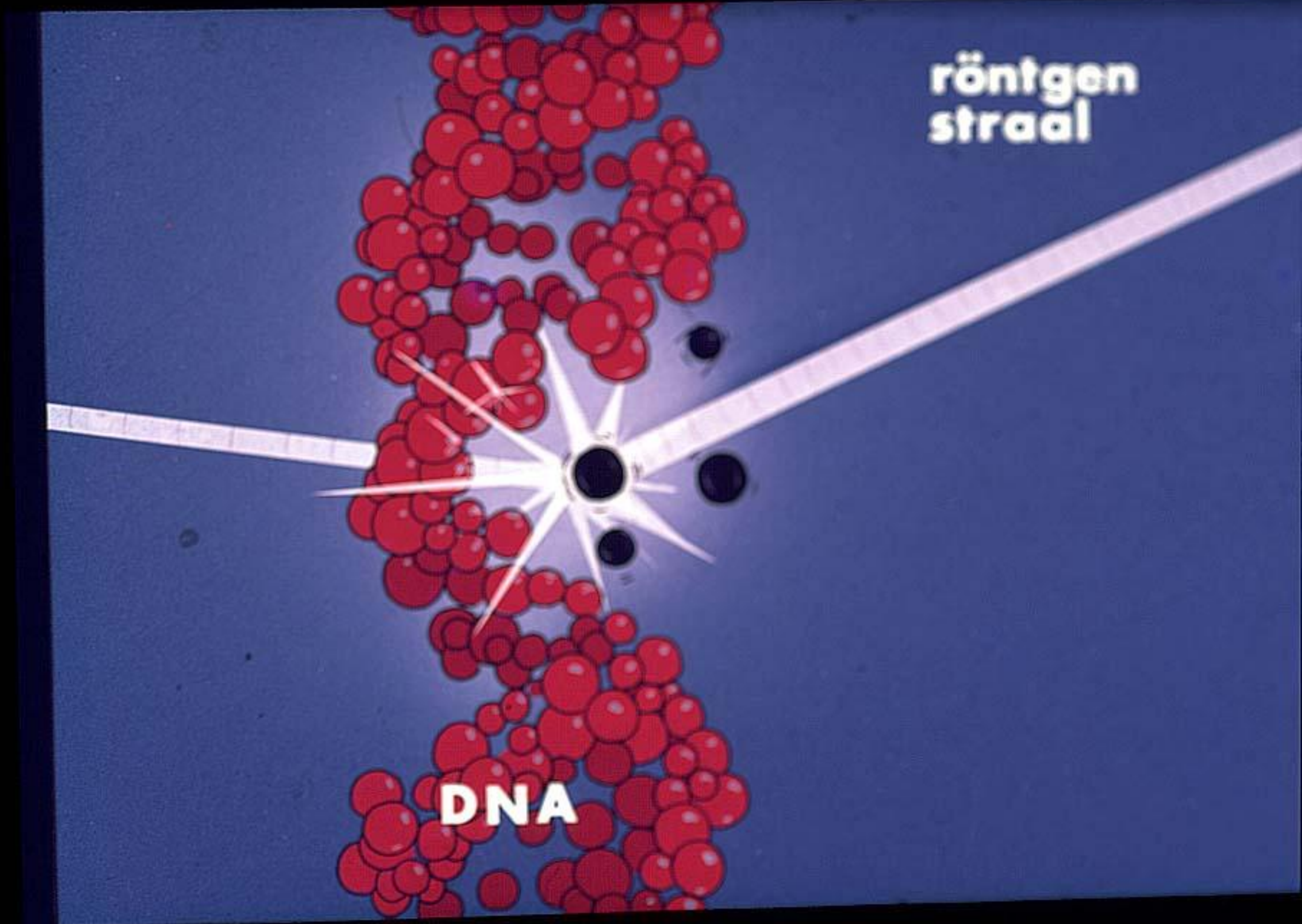
A CONTRIBUTION to the theory of warning colours and mimicry appears in the *Journal* of the Asiatic Society of Bengal (vol. lxv. Part ii. No. 1, 1896). Mr. Frank Finn, Deputy Superintendent of the Indian Museum, has tested the taste of the common garden lizard of India (*Calotes versicolor*) for various insects, and especially for butterflies protectively coloured and plain. Mr. Finn thinks the behaviour of the reptiles at liberty does not afford support to the belief that the butterflies, at any rate, usually considered nauseous, are distasteful to them.

WE understand that the next instalment of the "System of Medicine," which Prof. Clifford Allbutt is editing for Messrs. Macmillan and Co., will deal with Gynæcology, and will appear in the course of September. Dr. Playfair is associated with Prof. Allbutt as editor of this volume, which, though uniform with the system, will be complete in itself. The second volume of the "System of Medicine" proper may be expected by the end of the year. Messrs. Macmillan and Co. will also shortly issue a work on "Deformities," by Mr. A. H. Tubby. It is a comprehensive treatise on orthopædic surgery, and is fully illustrated by two hundred original plates and figures, and notes of one hundred cases.

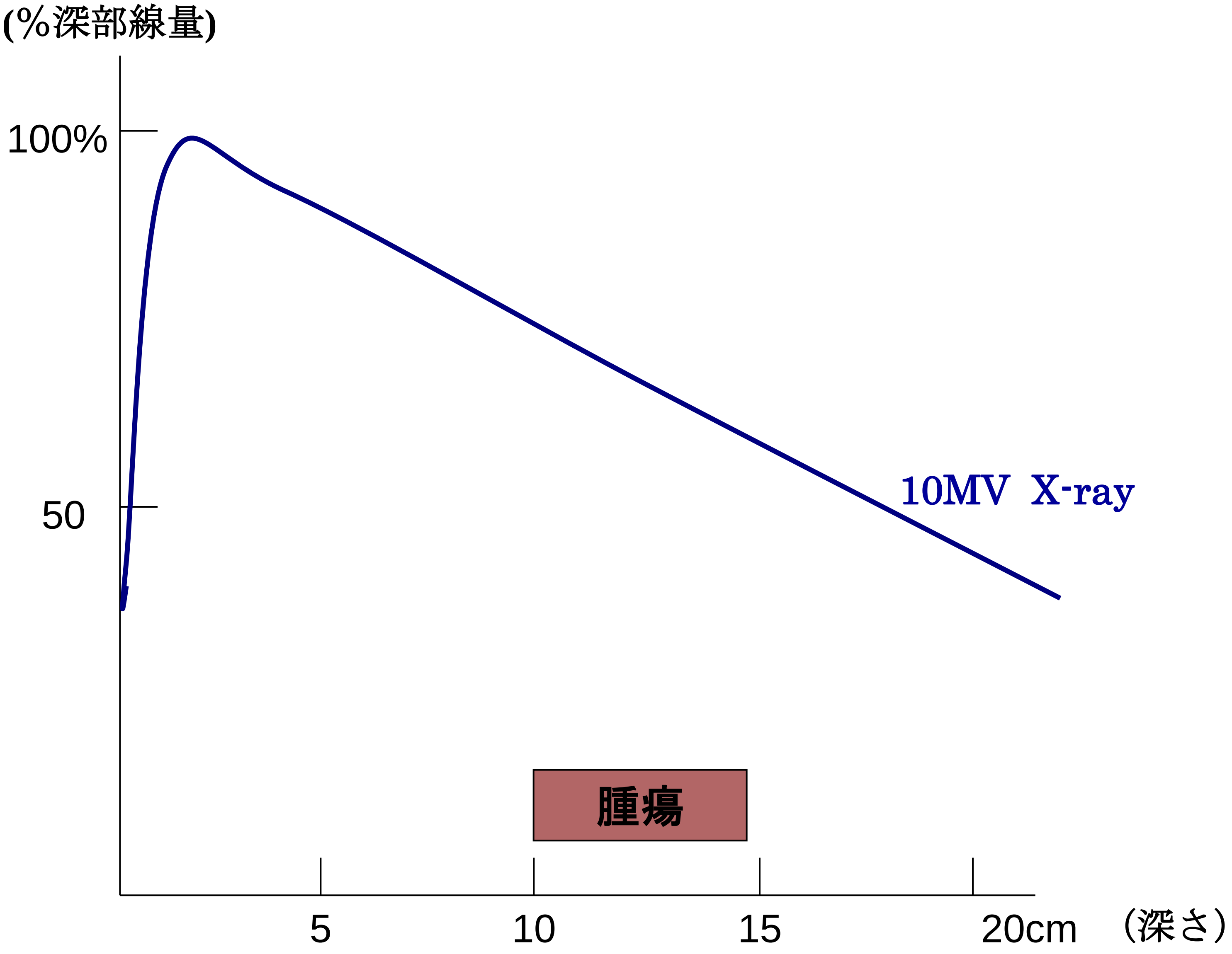
THE June number of the *Journal* of the Chemical Society is



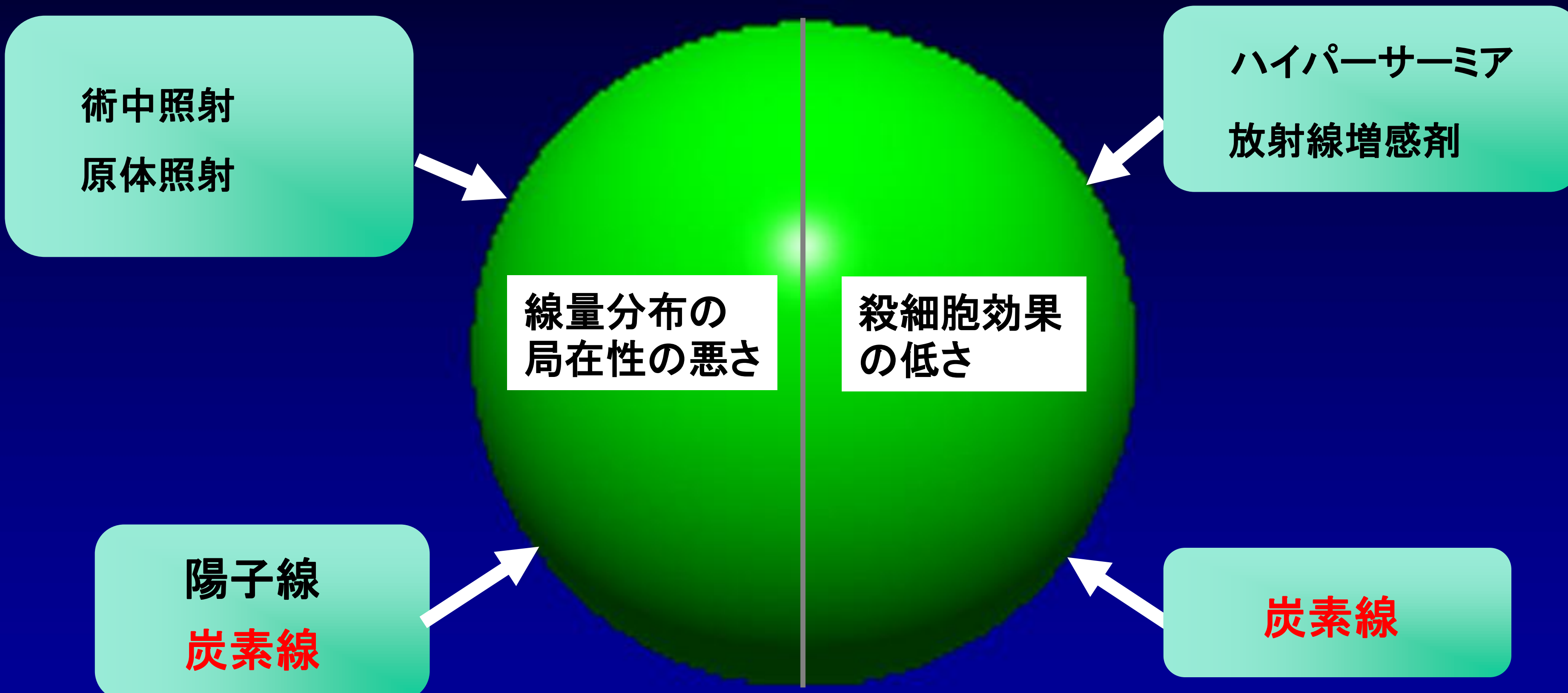

0 10 20 30 40 50

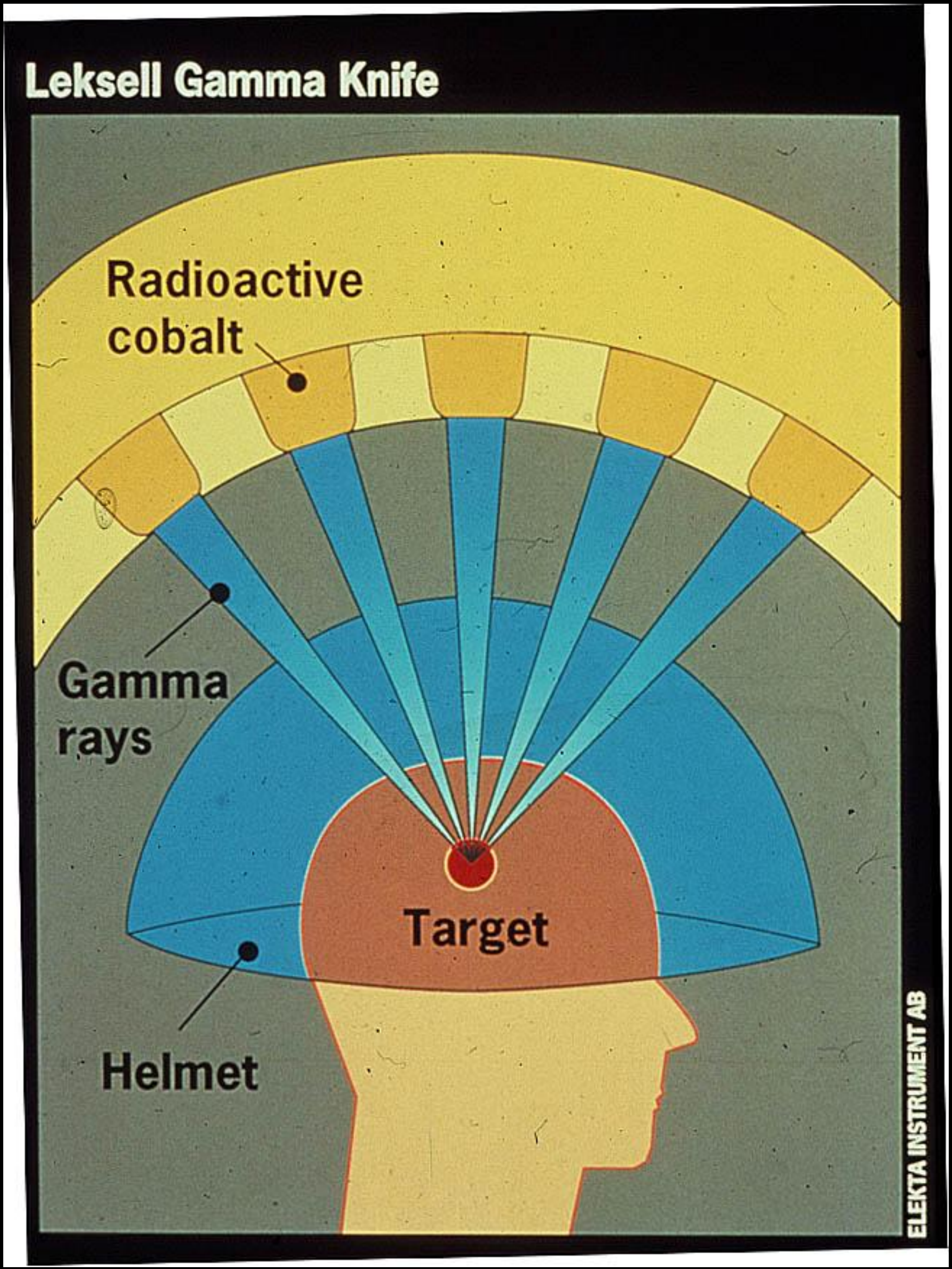

röntgen
straal
DNA

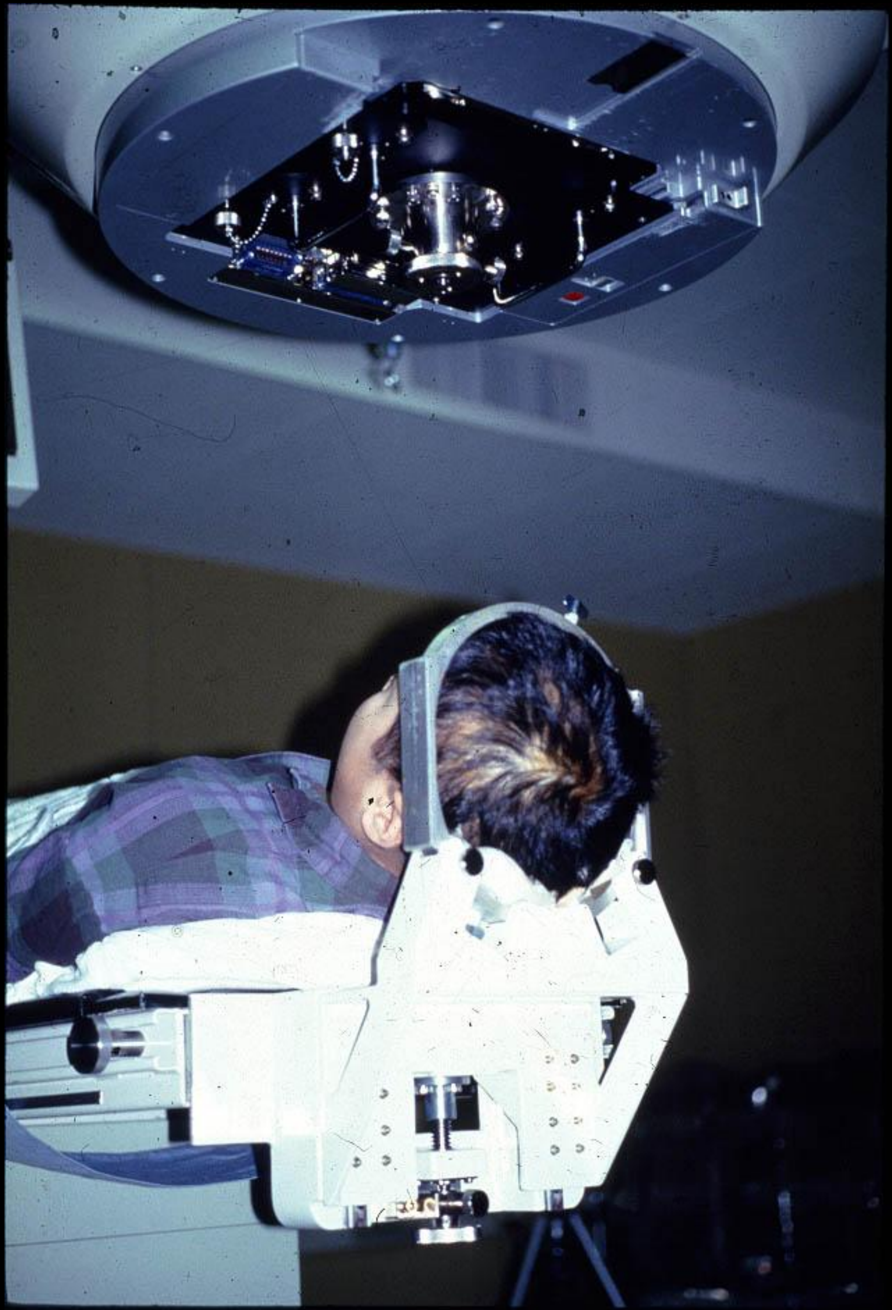
X線の線量分布



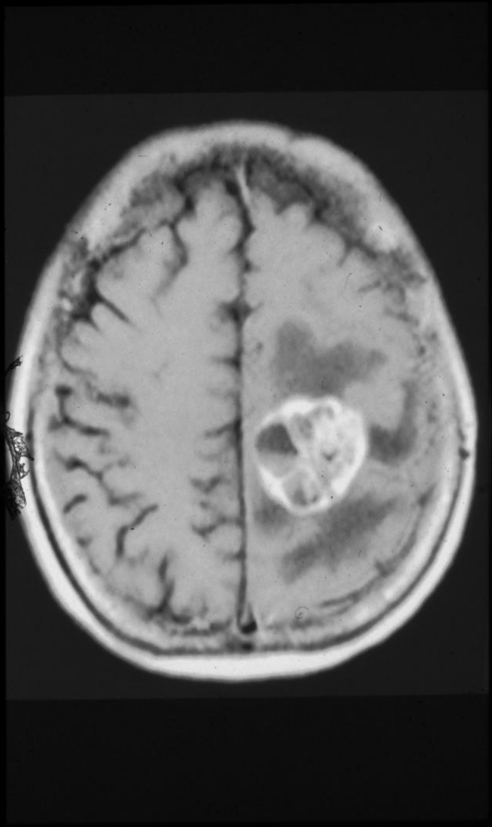
放射線治療の問題点と対策

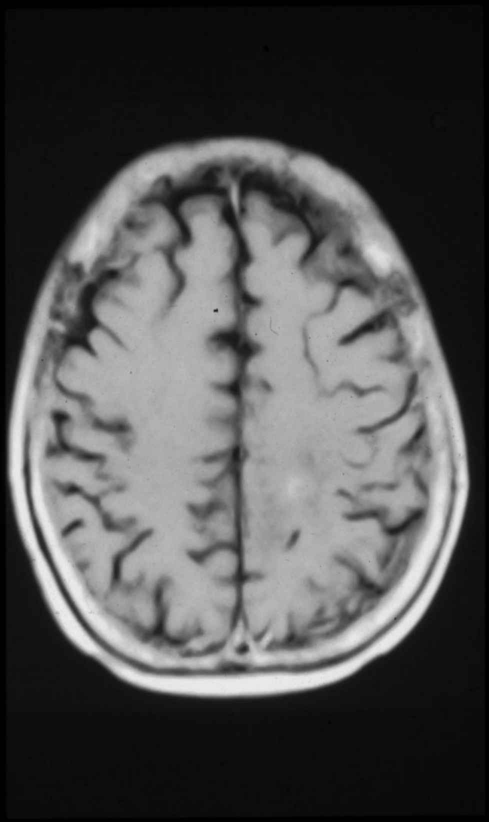



Leksell Gamma Knife
Radioactive cobalt
Gamma rays
Target
Helmet
ELEKTA INSTRUMENT AB



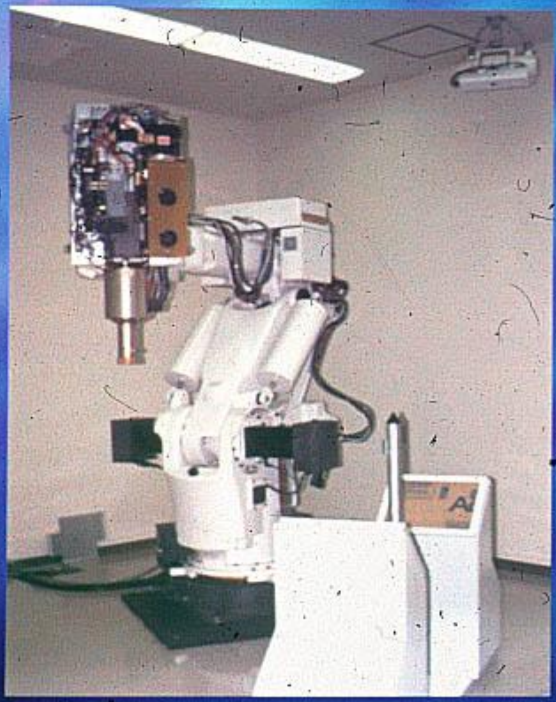
定位放射線照射



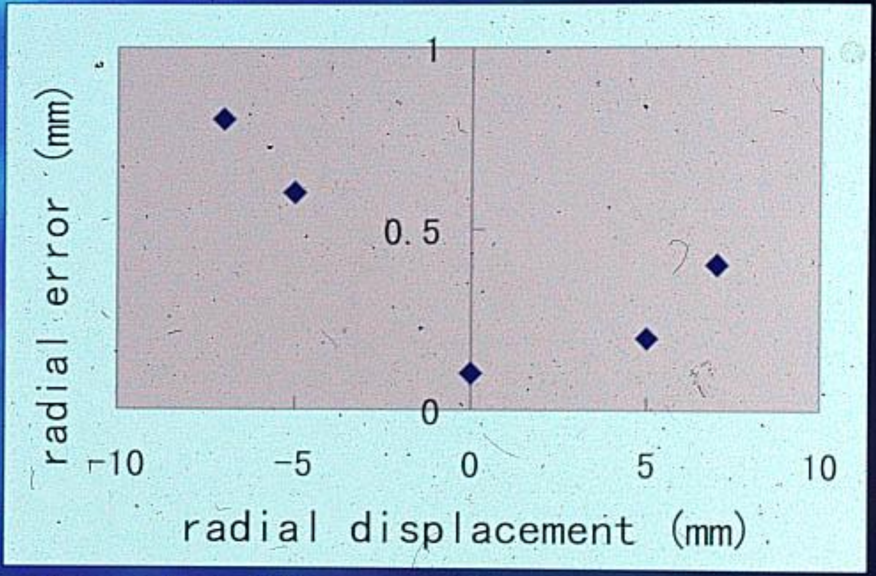


Tomotherapy（トモセラピー）

Cyberknife



ロボット
Beam Positioning Accuracy :
0.63 mm



トラッキング
Target Tracking Accuracy : less than 1 mm

将来性
脳、頭頸部以外の骨盤などに適応拡大

粒子線治療

放射線の種類

放射線
- X線、γ線 （光子線）
- 陽子線、炭素線（粒子線）

Radiological Use of Fast Protons

ROBERT R. WILSON

Research Laboratory of Physics, Harvard University

Cambridge, Massachusetts

EXCEPT FOR electrons, the particles which have been accelerated to high energies by machines such as cyclotrons or Van de Graaff generators have not been directly used therapeutically. Rather, the neutrons, gamma rays, or artificial radioactivities produced in various reactions of the primary particles have been applied to medical problems. This has, in large part, been due to the very short penetration in tissue of protons, deuterons, and alpha particles from present accelerators. Higher-energy machines are now under construction, however, and the ions from them will in general be energetic enough to have a range in tissue comparable to body dimensions. It must have occurred to many people that the particles themselves now become of considerable therapeutic interest. The object of this paper is to acquaint medical and biological workers with some of the physical properties and possibilities of such rays.

To be as simple as possible, let us consider only high-energy protons: later we can generalize to other particles. The accelerators now being constructed or planned will yield protons of energies above 125 Mev (million electron volts) and perhaps as high as 400 Mev. The range of a 125 Mev proton in tissue is 12 cm., while that of a 200 Mev proton is 27 cm. It is clear that such protons can penetrate to any part of the body.

The proton proceeds through the tissue in very nearly a straight line, and the tissue is ionized at the expense of the energy of the proton until the proton is stopped. The dosage is proportional to the ionization per centimeter of path, or specific ionization, and this varies almost inversely with the energy of the proton. Thus the specific ionization or dose is many times less where the proton enters the tissue at high energy than it is in the last centimeter of the path where the ion is brought to rest.

These properties make it possible to irradiate intensely a strictly localized region within the body, with but little skin dose. It will be easy to produce well collimated narrow beams of fast protons, and since the range of the beam is easily controllable, precision exposure of well defined small volumes within the body will soon be feasible.

Let us examine the properties of fast protons somewhat more quantitatively. Perhaps the most important biological quantity is the specific ionization, or number of ions per centimeter of track. This quantity is not difficult to calculate. The results of such calculations are shown in Figure 1, where the range of protons in tissue is plotted for protons of various energies. In the same figure, the specific ionization is plotted as a function of the range in tissue. For purposes of calculation, tissue has been assumed to have the molecular formula (1): $C_{0.5}H_8O_{3.8}N_{0.14}$, and to be of unit density, *i.e.*, 15 per cent protein and 85 per cent water. The calculations can be easily extended to other materials and densities.[2] The accuracy is perhaps 5 per cent. However, exact values for various tissues can be quickly measured as soon as the fast protons are available.

Figure 1 shows, for example, that if we want to expose a region located 10 cm. be-

[1] Accepted for publication in July 1946.

[2] The range of a proton in air in meters is given by the convenient formula $R = (E/9.29)^{1.8}$ where the energy is expressed in Mev. The range in tissue is 1.11×10^{-3} times the range in air. The stopping power of other substances may be found in Livingston and Bethe: Rev. Mod. Physics 9: 246, 1937. The physical calculations of this paper will be submitted to the *Physical Review* for publication.

millionths of an erg, each proton loses 48 millionths of an erg in the last centimeter. Hence, to produce 1 r.e.d. averaged over the last centimeter of depth requires $83/48 \times 10^6 = 1.72$ million protons per square centimeter. To produce 1,000 r.e.d. will require 1.72 billion protons per square centimeter. This corresponds to a current of 2.75×10^{-10} amp./cm.^{2} of protons for a one-second exposure or 4.6×10^{-13} amp./cm.^{2} for a ten-minute exposure.[3] The machines now under construction should have little difficulty in producing such currents. In fact, it is expected that they will yield currents millions of times as great. It will be simple to collimate proton beams to less than 1.0 mm. diameter or to expand them to cover any area uniformly.

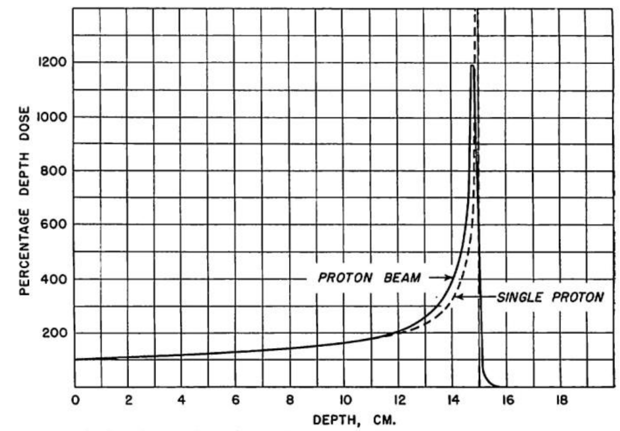


Fig. 2. The dotted curve shows the relative dose due to a single 140 Mev proton. The full curve shows qualitatively the depth dose curve for a beam of 140 Mev protons in tissue.

Let us now become a little more technical and consider secondary effects. First, the energy loss of the proton is a statistical effect due essentially to the production of ions along its path; hence, not all protons of the same energy will stop at the same distance beneath the skin. This effect is called range straggling and is easy to calculate. The results of such calculations can be summarized by saying that the longitudinal width in which most protons come to rest is about 1 per cent of the initial range.[4] The effect of this on the depth dose curve is qualitatively shown in Figure 2. As a result of straggling, the full curve obtains instead of the dotted one.

A second effect is due to the many small

[3] More generally the r.e.d. at a point x cm. below the surface is given approximately by the formula

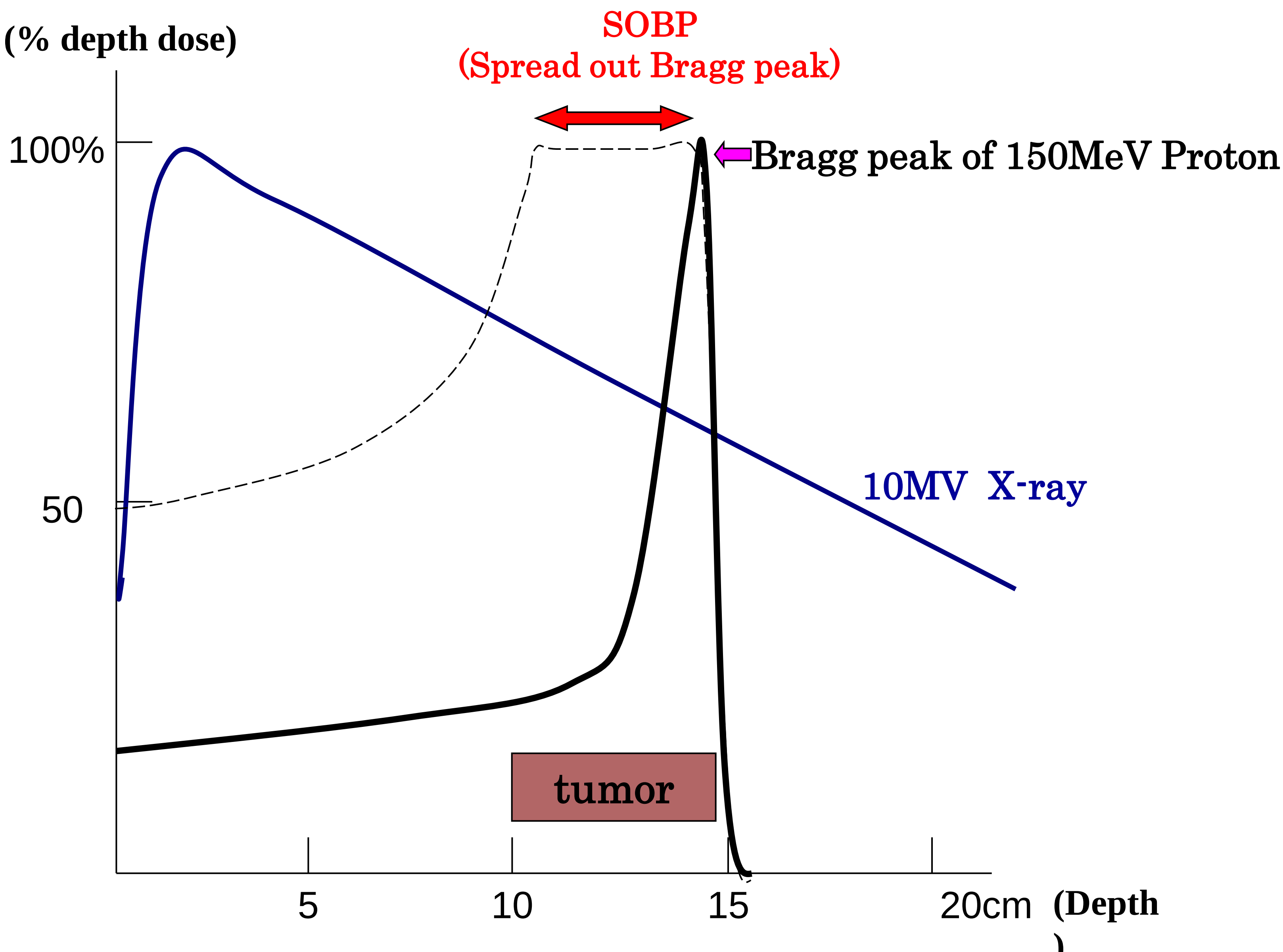
$$\text{r.e.d.} = 4.8 \times 10^{10} \frac{jt}{(R - X)^{0.444}}$$

where R is the total range of the proton in tissue in cm., j the current density or protons in amperes/cm^2., and t the exposure time in seconds. The formula is not accurate in the last millimeters of range.

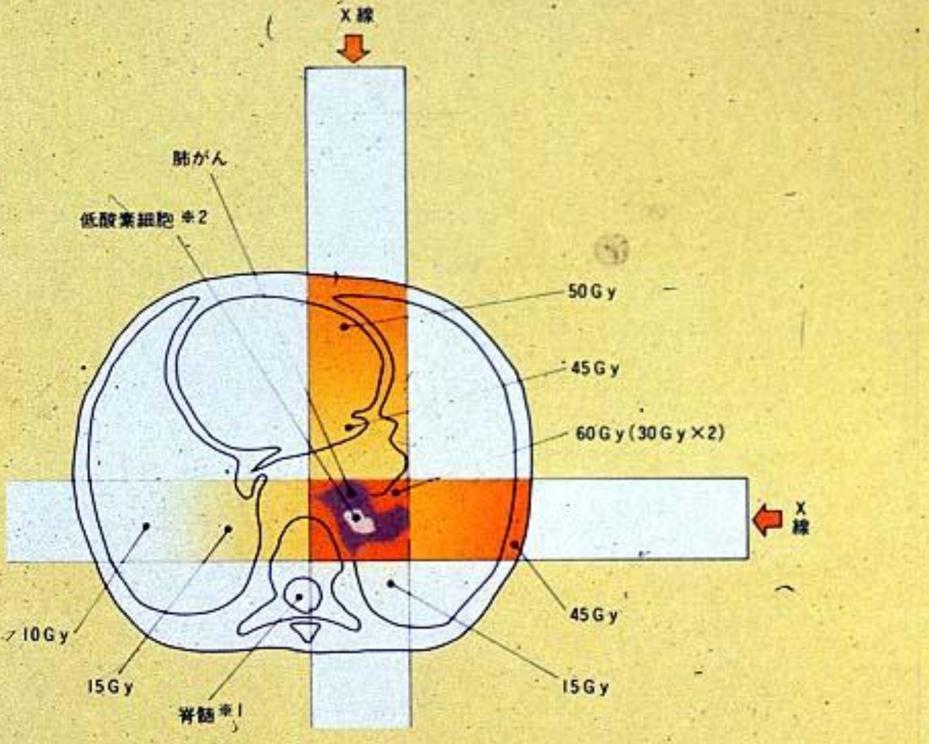
[4] The protons come to rest so that the distribution of their end-points is given by $P(x)dx = \frac{R}{\alpha\sqrt{\pi}} e^{-\frac{(R-x)^2}{R^2\alpha^2}} dx$, where x is the distance below the surface, and α is given by

$$\alpha = \frac{7.1}{E_0^{1/2}} \left(\frac{NZz^2R}{E_0}\right)^{-0.055}$$

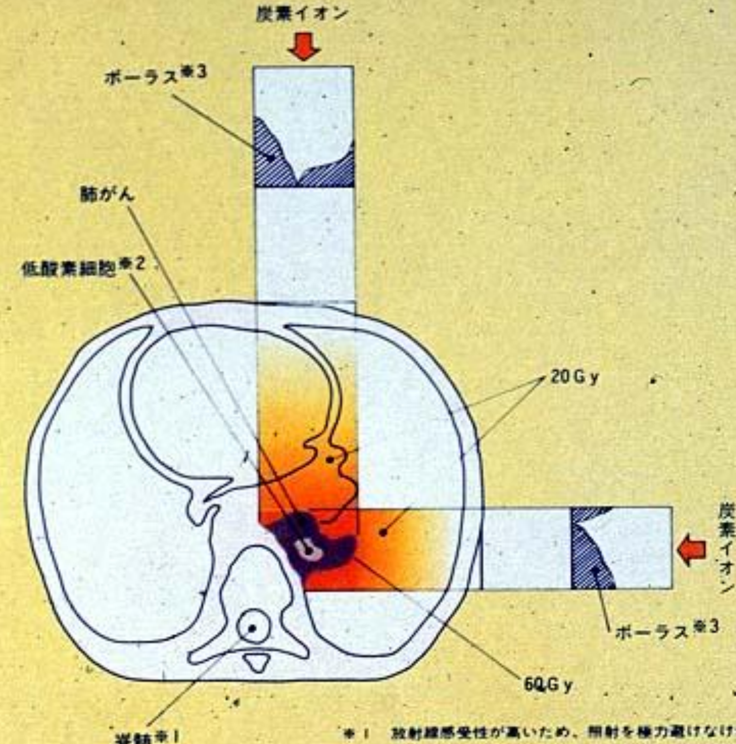
where N is the atoms per cm.^{3}, Z is the atomic number, z is the ion charge number, E_0 is the rest energy of the ion in Mev, and R is the range in cm.



(% depth dose)
SOBP
(Spread out Bragg peak)
100%
Bragg peak of 150MeV Proton
50
10MV X-ray
tumor
5
10
15
20cm
(Depth
)



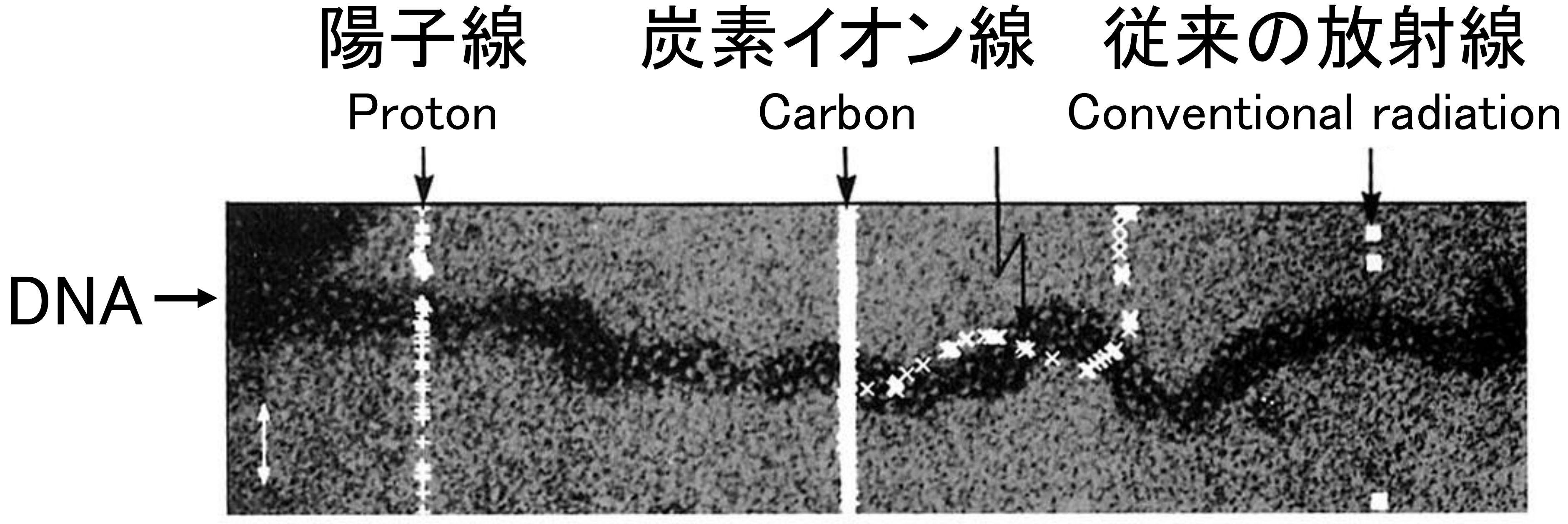
※1　放射線感受性が高いため、照射を極力避けなければならない臓器
※2　がん細胞のうち、放射線感受性が低く従来の放射線（X線、γ線）で殺傷することが困難な細胞



※1　放射線感受性が高いため、照射を極力避けなければならない臓器
※2　がん細胞のうち、放射線感受性が低く従来の放射線（X線、γ線）で殺傷することが困難であった細胞
※3　放射線線量分布をがんの形に合わせて調整するための補正材

粒子線治療の特徴
Feature of particle radiotherapy

優れた生物学的効果（DNA損傷効果）
Excellent biological potency (effect of DNA damage)



Hyogo Ion Beam Medical Center

粒子線治療の特徴

Feature of particle radiotherapy

- **優れた線量分布**
- Excellent dose distribution

物理学
physics

- **優れた生物学的効果**
- Excellent biological potency

生物学
biology

切らずに治すがん治療

Cancer treatment cured without surgical procedure

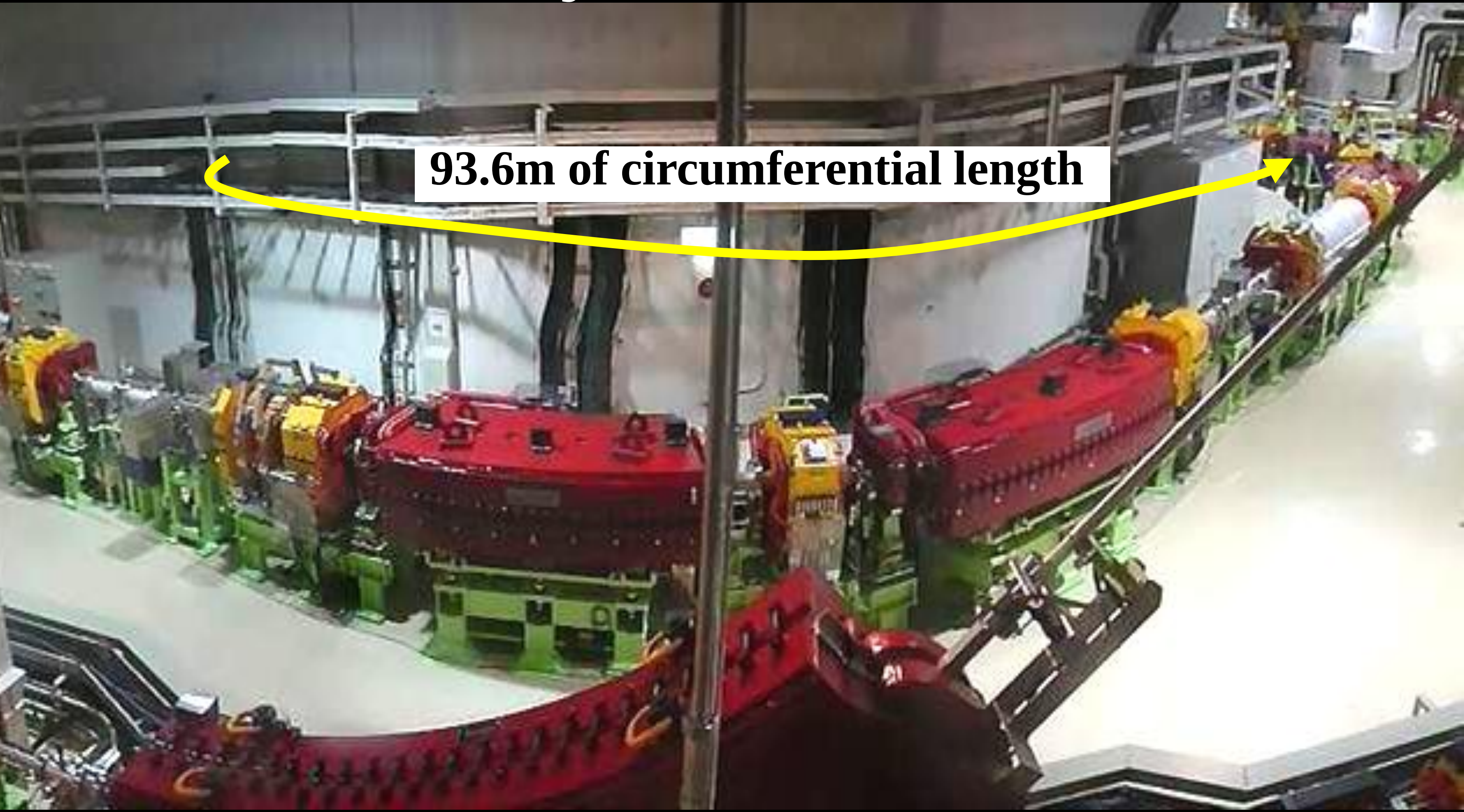

R
CHEVROLET

Hyogo Ion Beam Medical Center

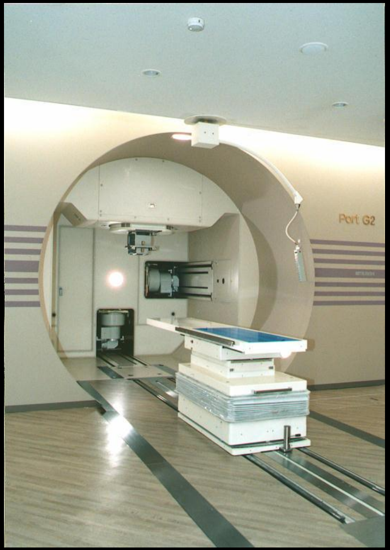
播磨科学公園都市

所在地：揖保郡新宮町光都
相生駅からバスで30分

Synchrotron



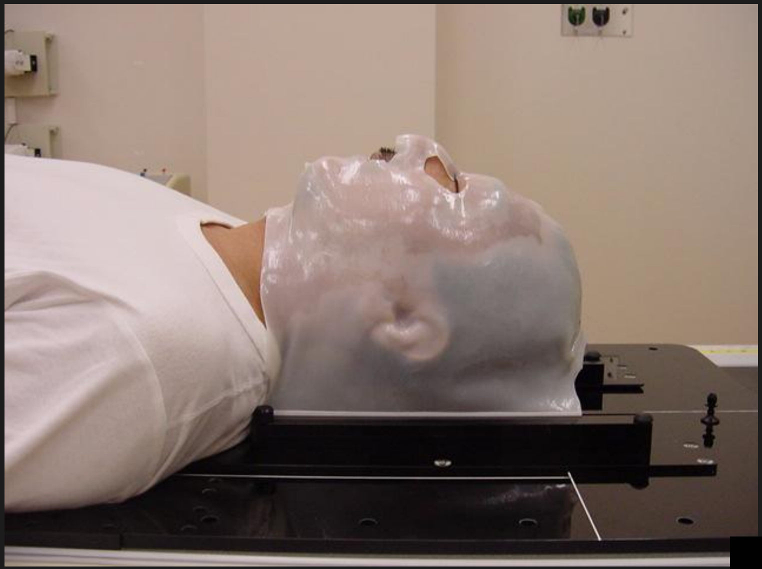
粒子線治療装置



照射装置

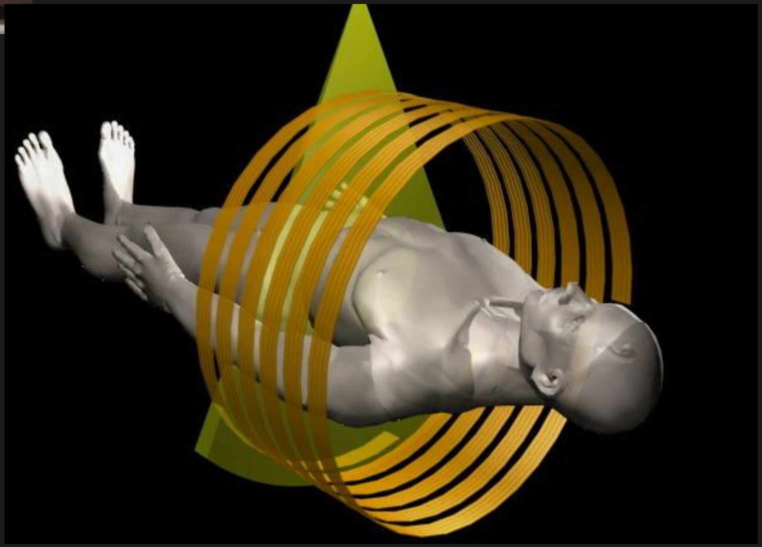
粒子線治療

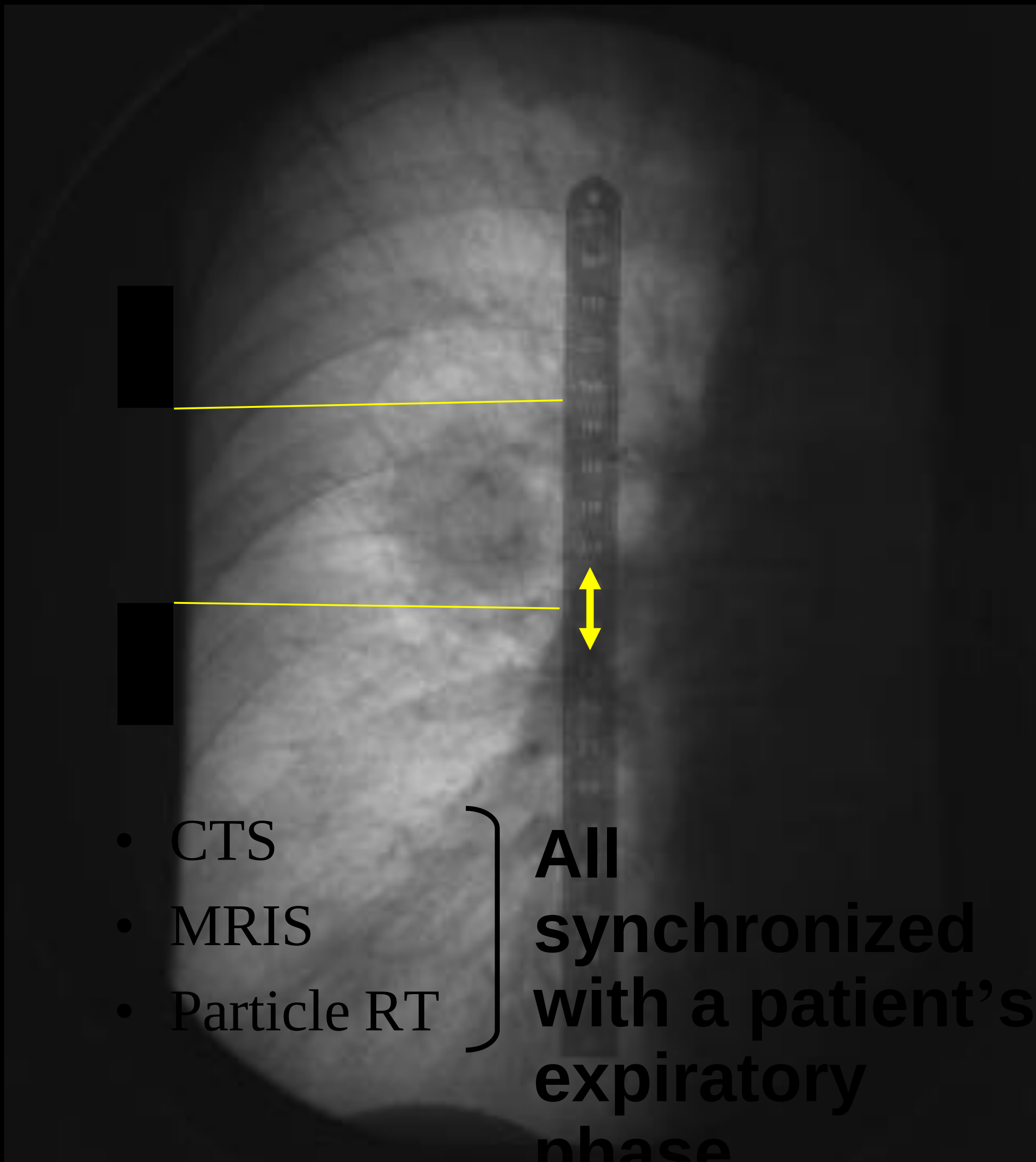
データ収集



固定具作成

CT,MRI撮影

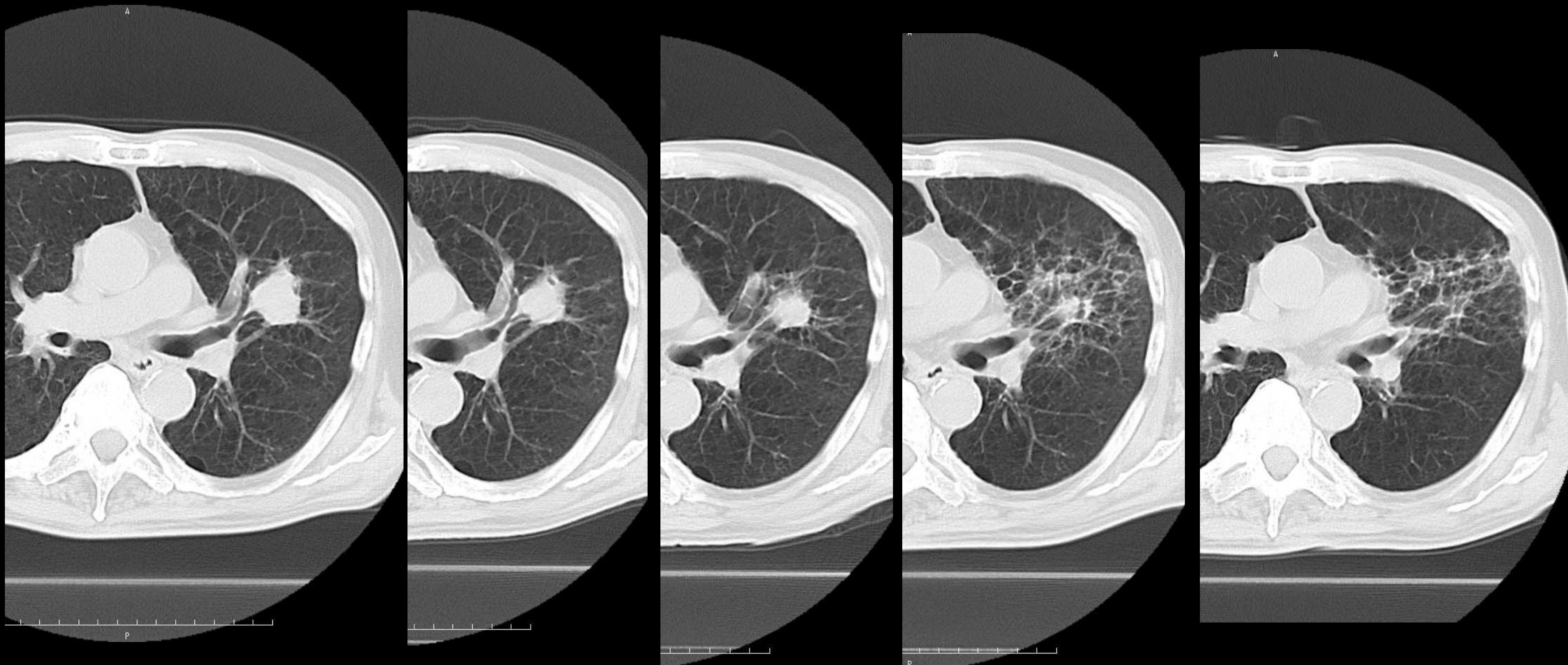




- CTS
- MRIS
- Particle RT

All synchronized with a patient's expiratory phase

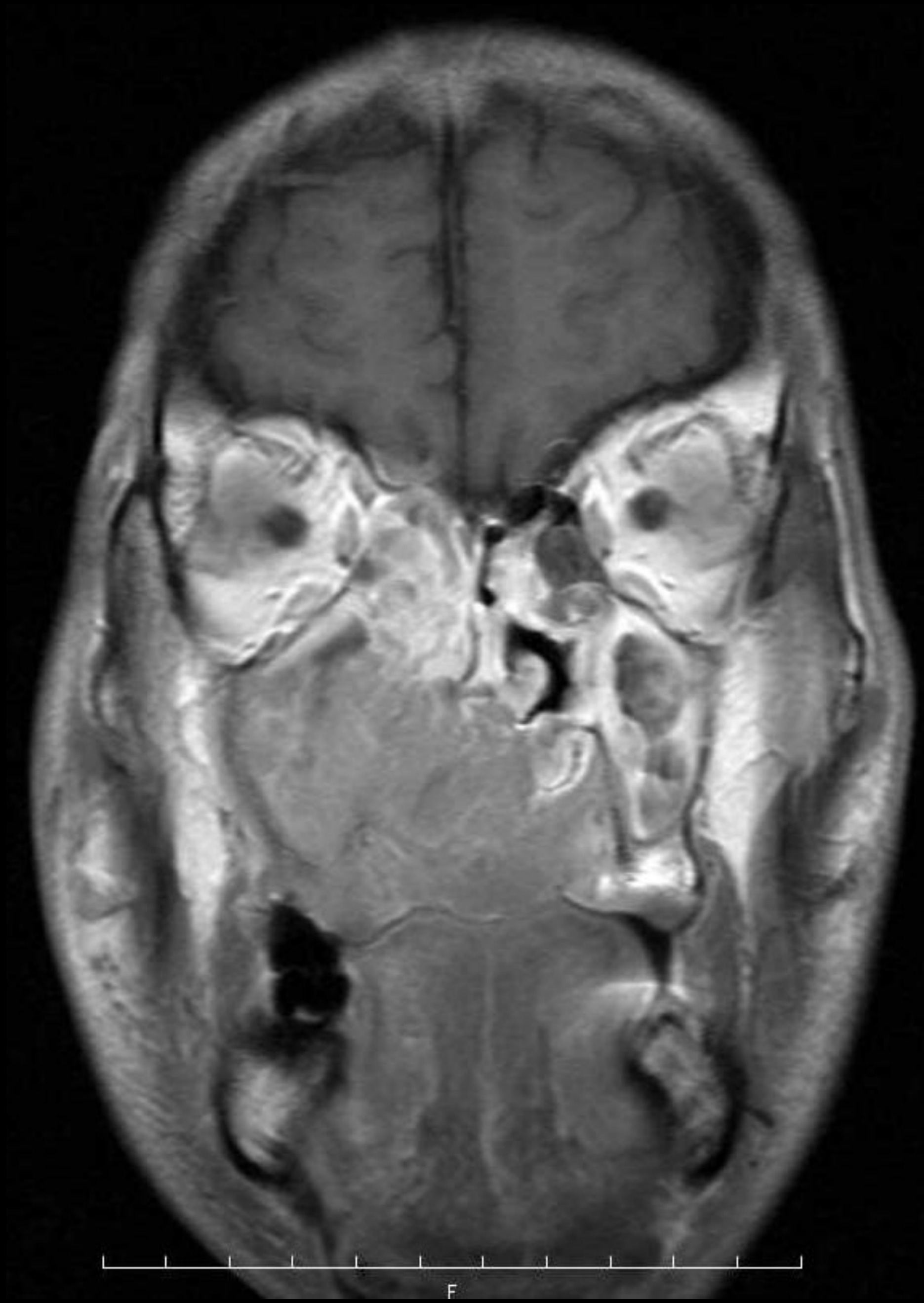
77y Male LC SqCCa T1N0M0 80GyE/20fr/5w



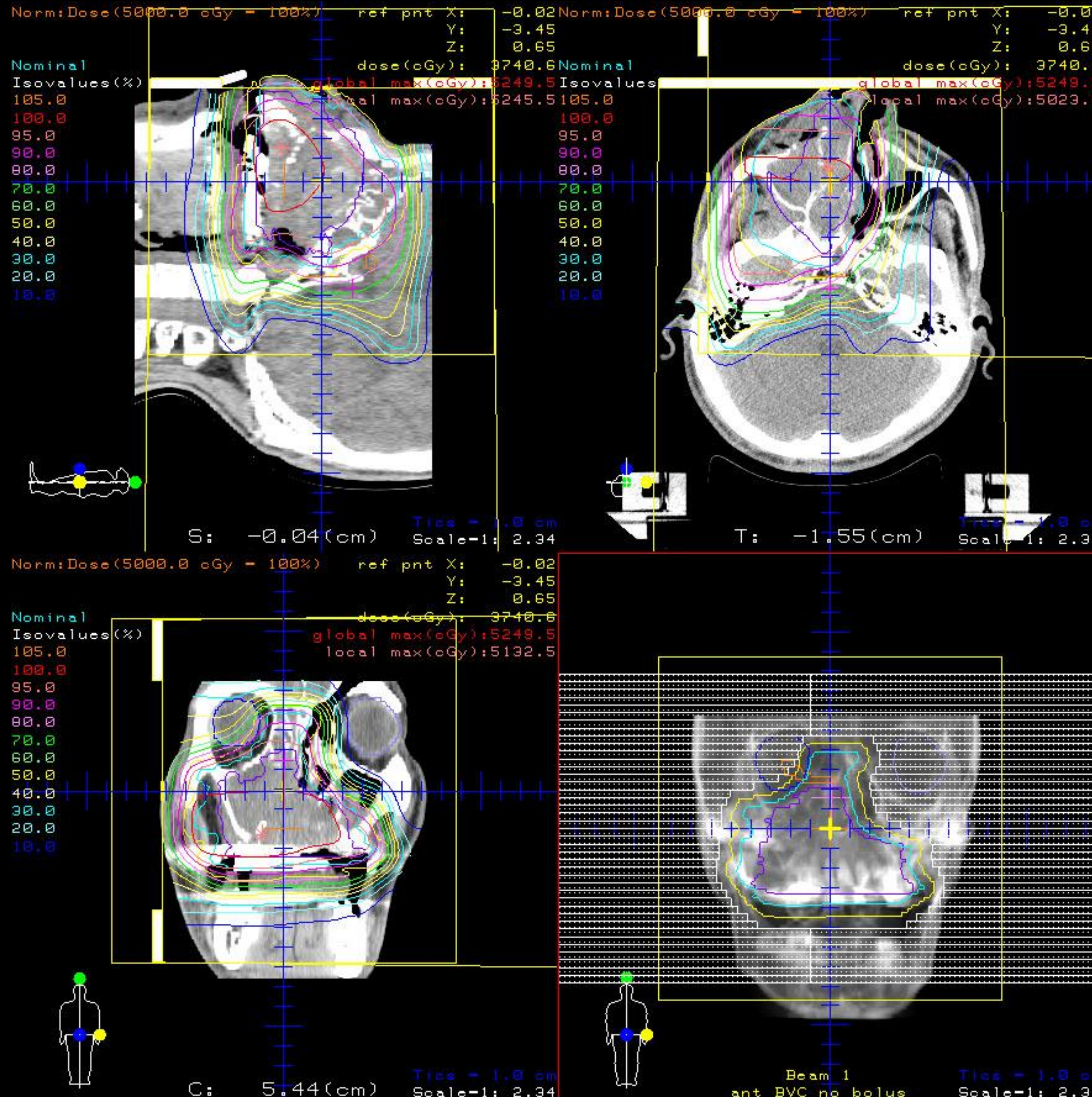
Before	52GyE	80GyE	2W	1M CR
PaO2 82 mmHg		78	80	81

Hyogo Ion Beam Medical Center

54y Male
Maxillary sinus CA
T4pN1M0

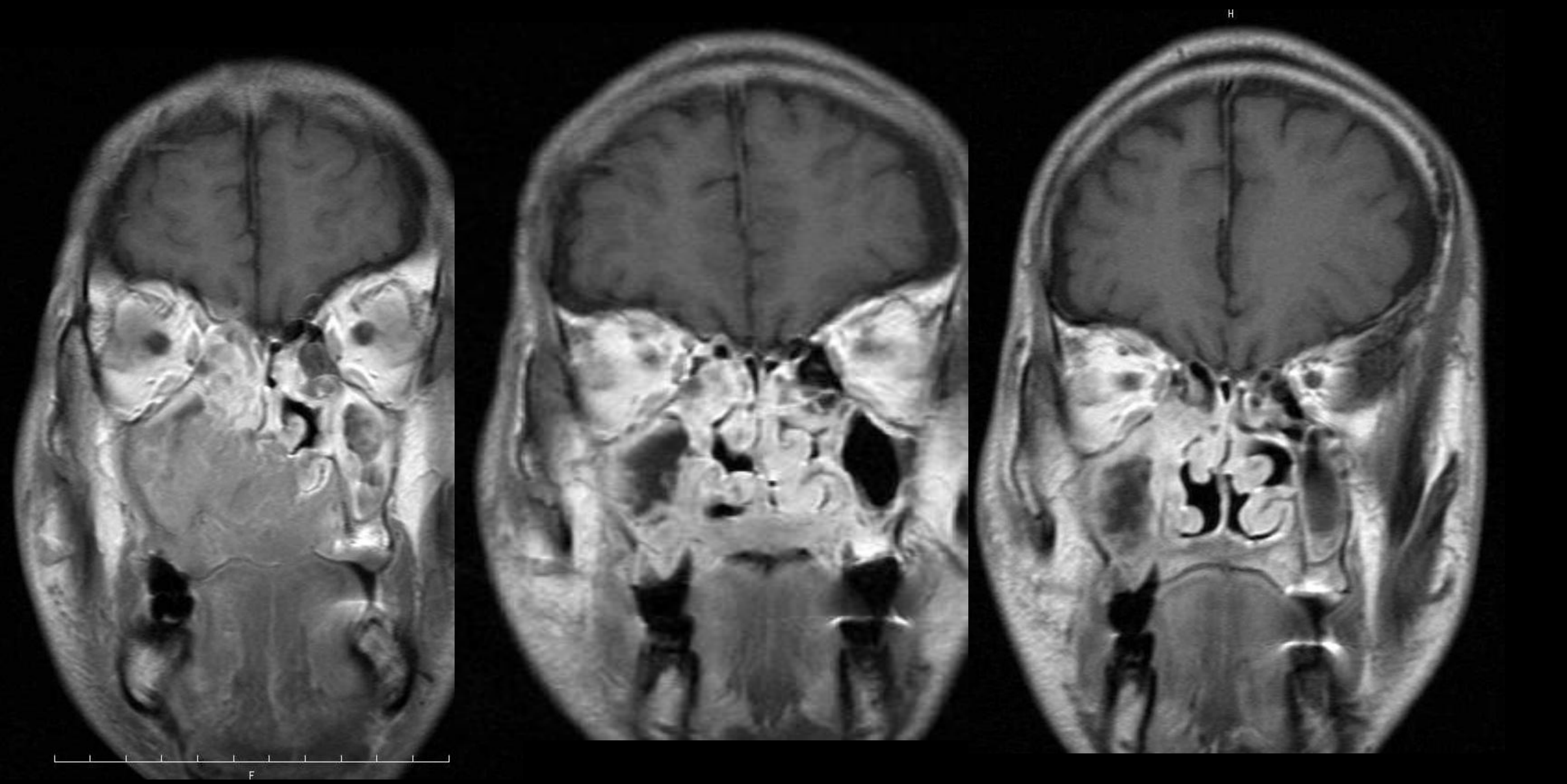


54y Male
Maxillary sinus CA
T4pN1M0
65GyE/26fr/7w



Hyogo Ion Beam Medical Center

54y Male Maxillary sinus CA T4pN1M0 65GyE/26fr/7w



Before **37.5GyE** **5M**

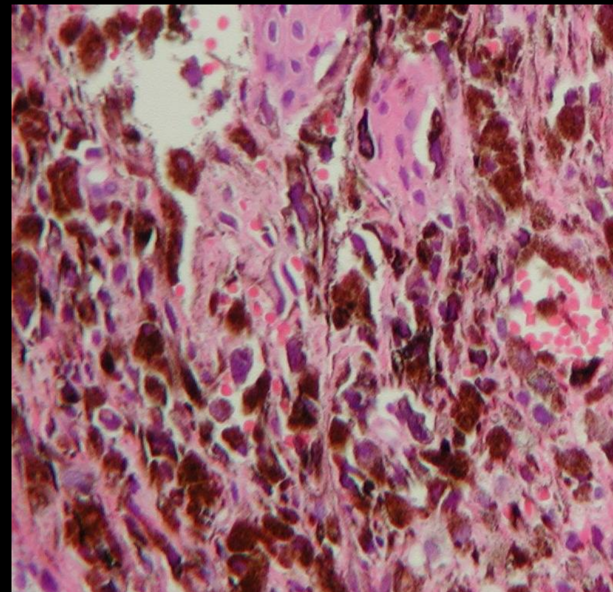
54y.o. Male
Maxillary sinus CA
T4pN1M0

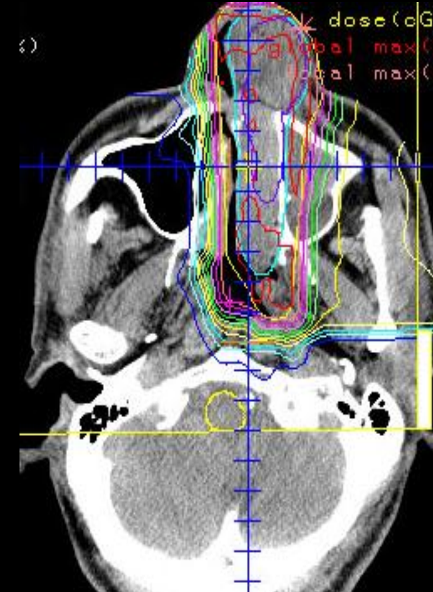
Proton 65 GyE mucosa = 32.5-61.8 GyE

Before	**35 GyE Grade2**	**1 Mo**
0.7	**1.1**	**0.2**

CRP (0-0.6 mg/dL)

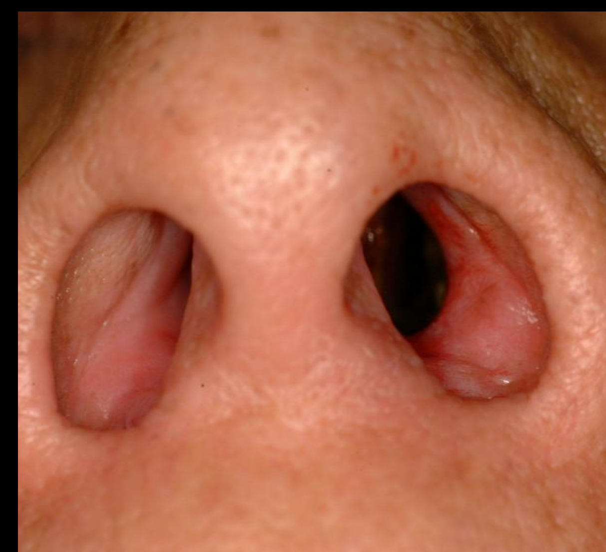
68M
左鼻腔　悪性黒色腫
(T3N0M0) Melanotic
炭素 57.6GyE/16回/4週





治療前

終了後4週(一次効果: PR)



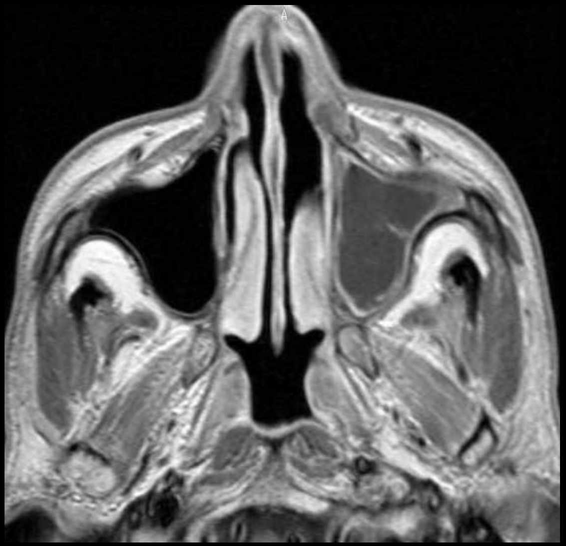
開始後5か月

Hyogo Ion Beam Medical Center

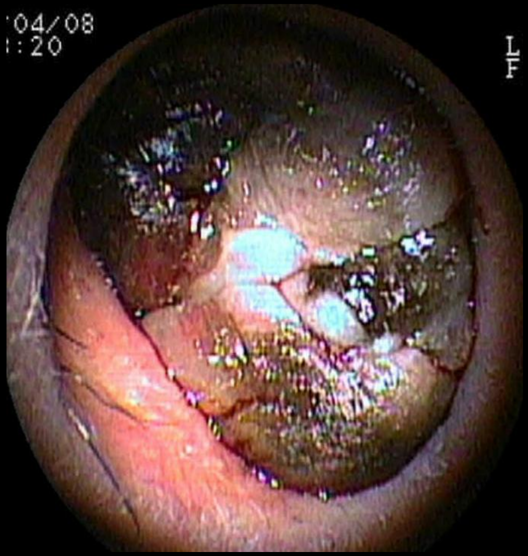
#3 68M
左鼻腔 悪性黒色腫
(T3N0M0)
Melanotic

炭素 57.6GyE/16回/4週

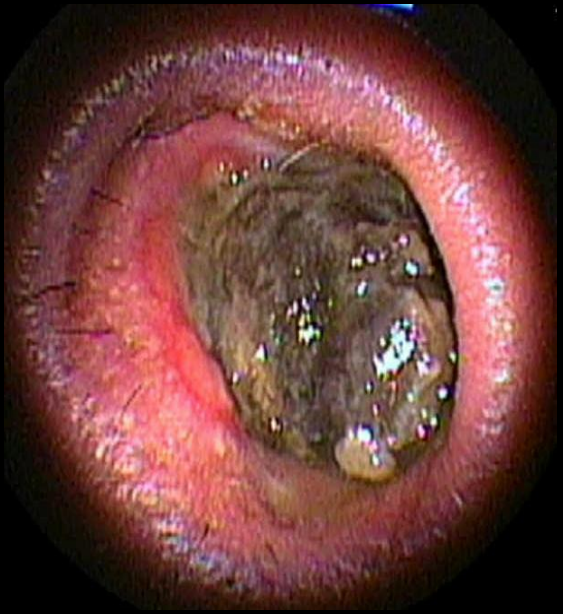
治療前



開始後8か月



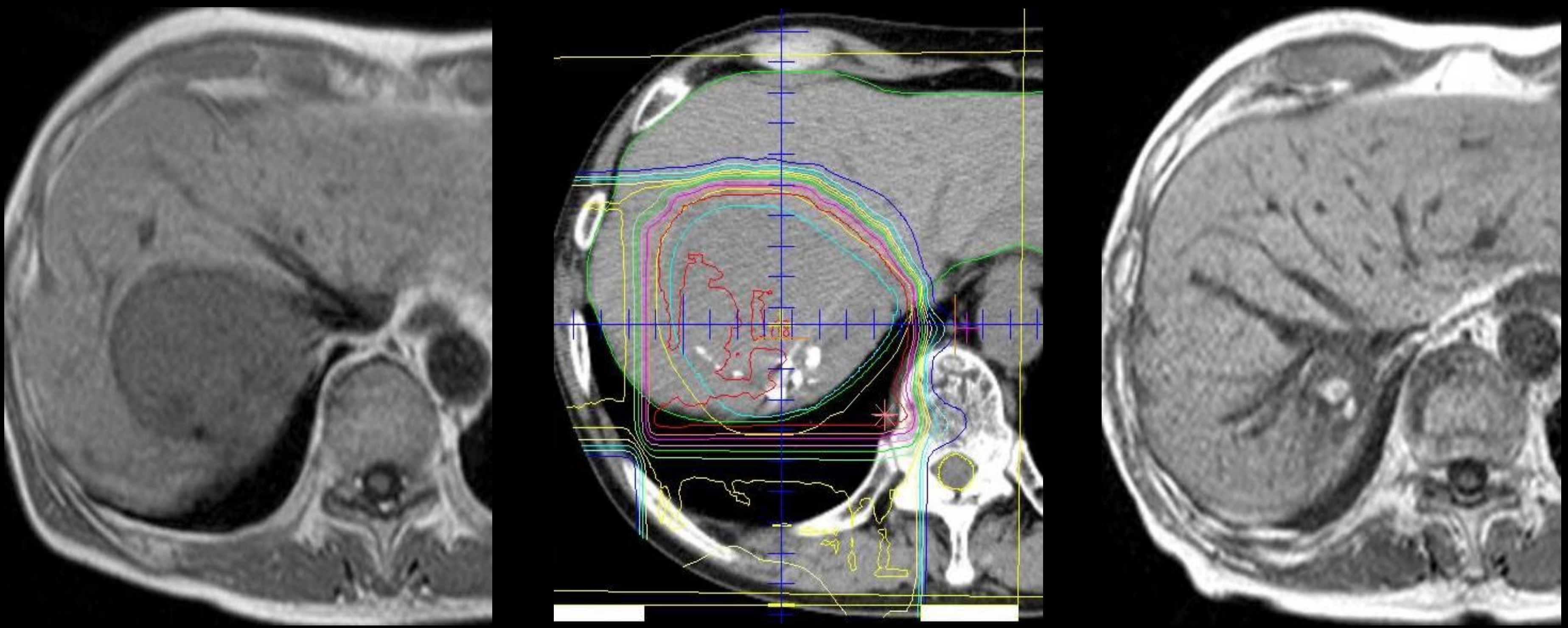
治療前



終了後4週(一次効果: PR)

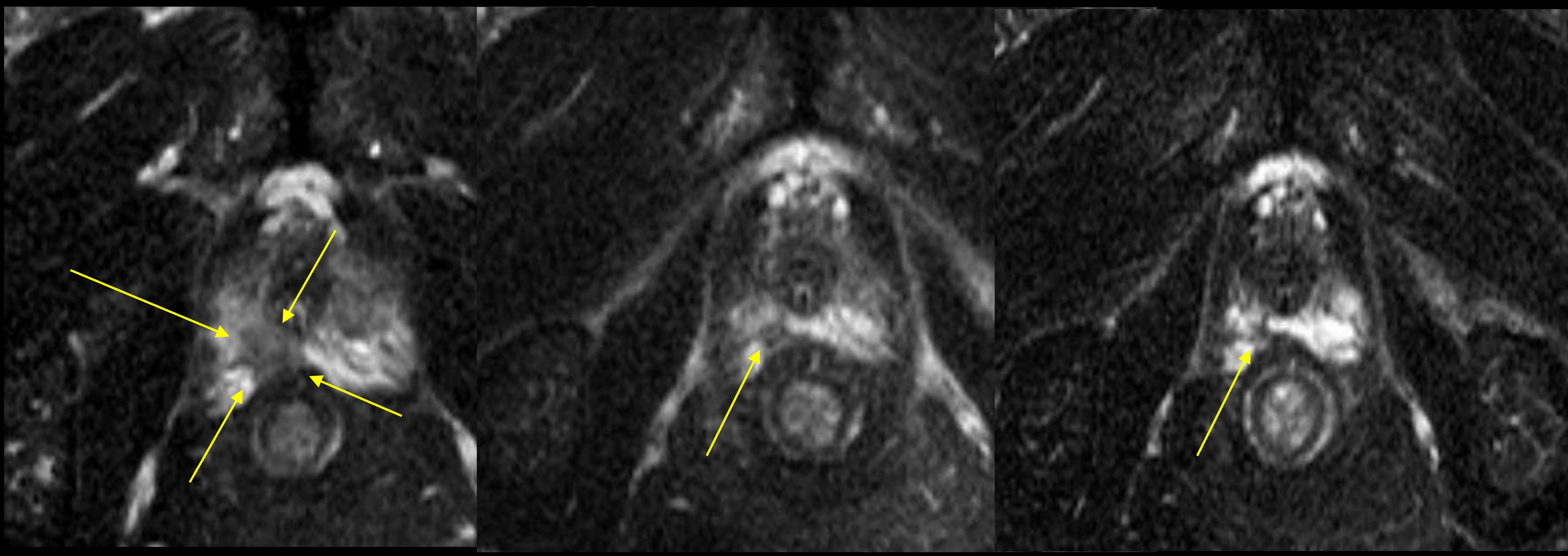
開始後8か月

Hyogo Ion Beam Medical Center



血液PIVKA-II　6110（正常値40以下）

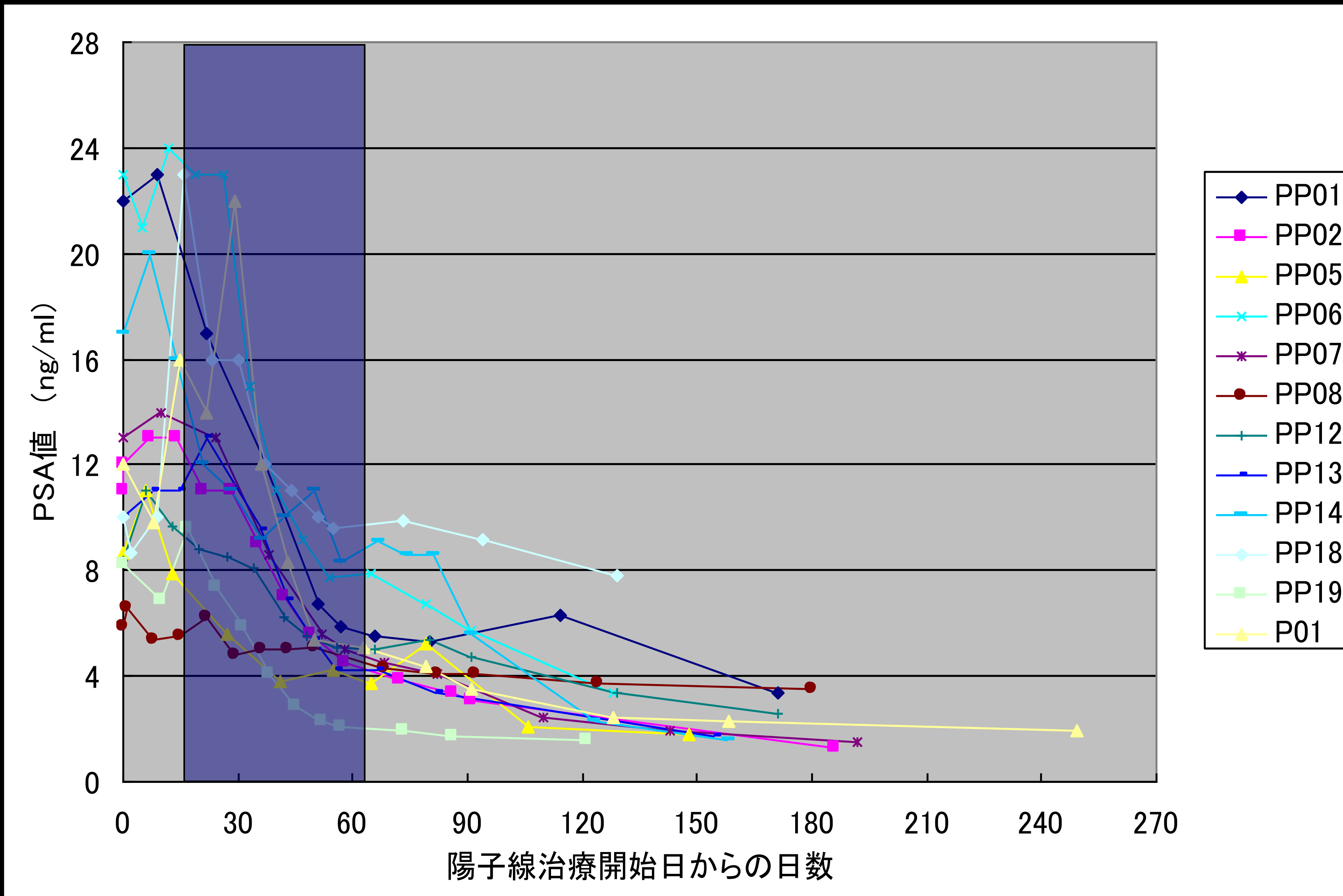
82y.o. Male Prostate CA T2aN0M0 74GyE/37fr/8w



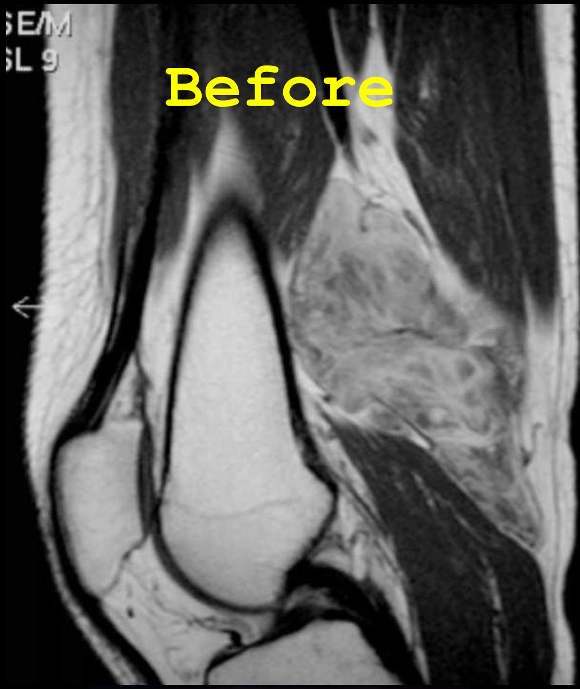
Before	48GyE	1M
13	8.6	4.5

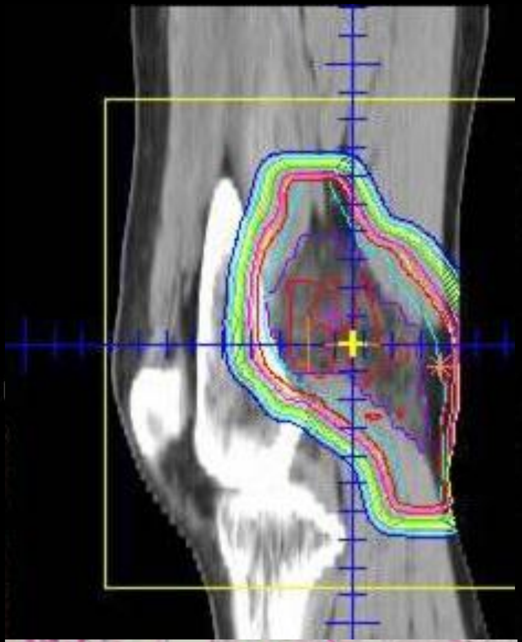
PSA (tandem-R: 0-4.0ng/mL)

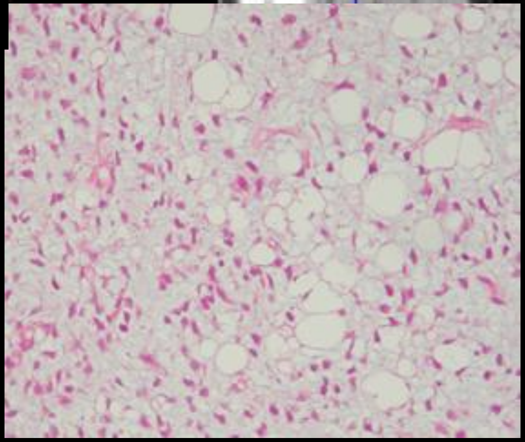
前立腺がんT1T2N0M0新鮮例のPSA変化

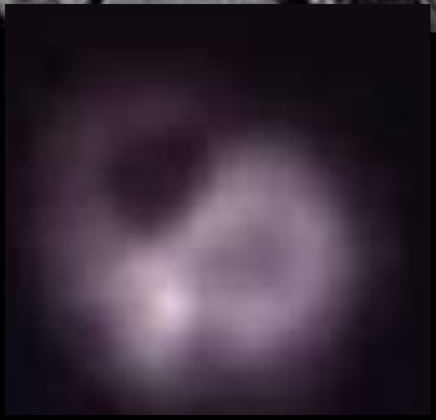


29F: Myxoid Liposarcoma



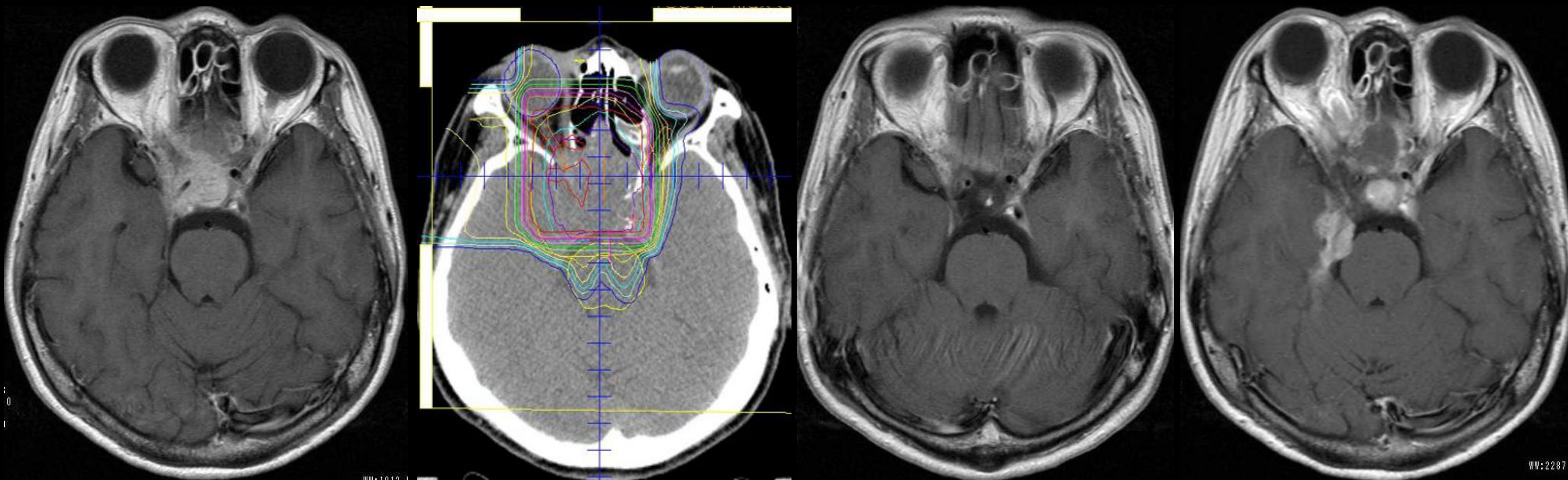






C10 58F Rt. Sphenoid Sinus CA T4N0M0 adenoidcysticCA

2/2



Before | Carbon Ion 57.6 GyE | 2 Mo | 6 Mo

Marginal Failure → **Radiosurgery (γ-knife)**

治療症例

患者さん

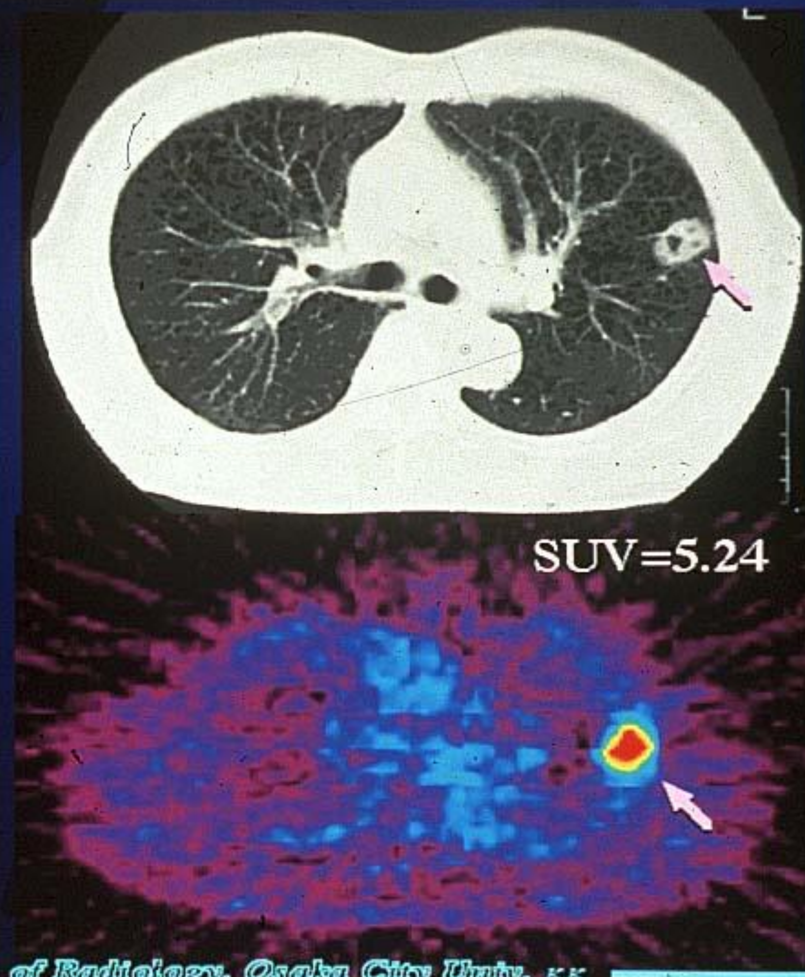
治療期間中の患者さん


SIMPSON SPORTS
We love golf

primary lung cancer
(lt. S^{1+2})

(poorly differentiated squamous cell carcinoma)

63 years old male



(August, 1999)

粒子線治療の長所と短所

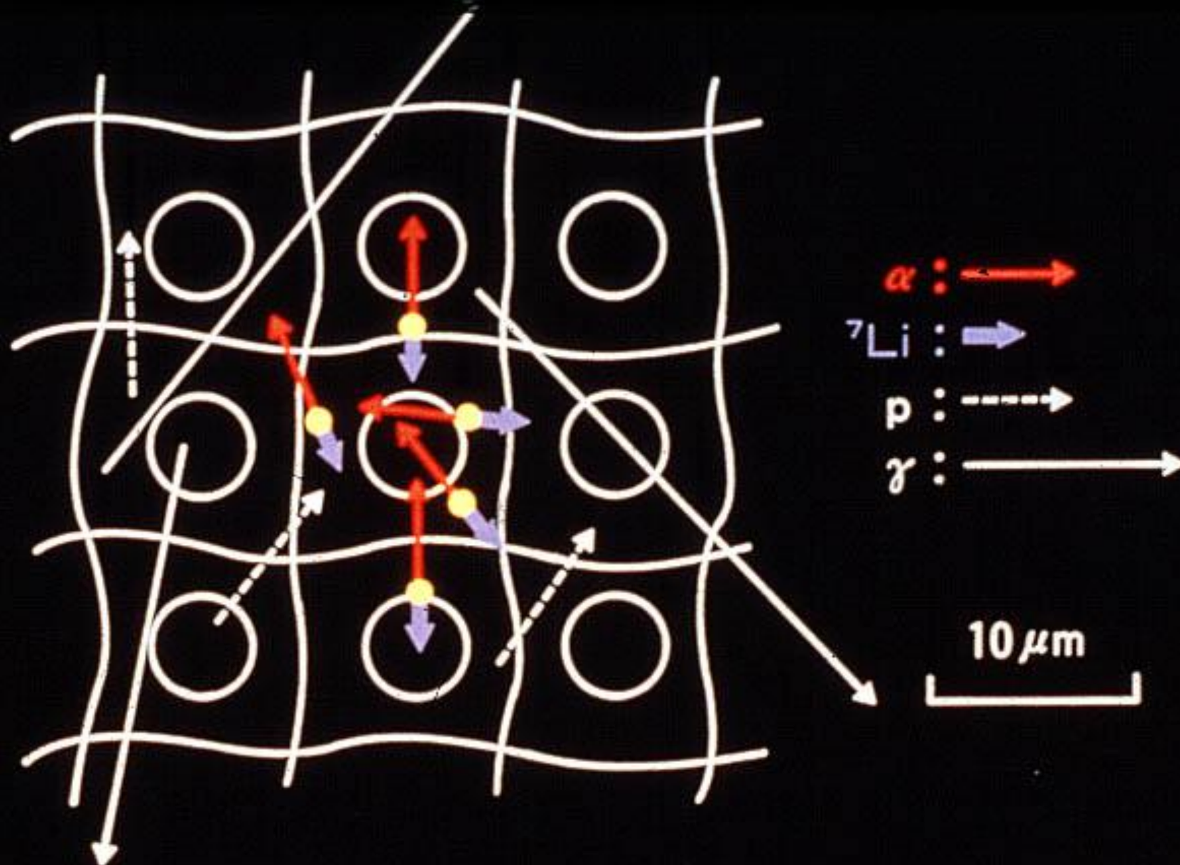
長所

- 患者にやさしい治療 （**痛みや苦痛が少ない**）
- 比較的早期の原発癌であれば、切らずに治癒可能 （**手術と比較して遜色がない**）
- 副作用が少なくQOL（生活の質）が高い。
- 速やかな社会復帰が可能
- 高齢者の場合、苦痛の少ない生き甲斐のある人生を送ることができる。

短所

- 胃癌や腸に近接しているがんは適応にならない。
- 治療費が約300万円と高額で、現在のところ自己負担である。
- 治療施設が2008年現在、7カ所と限られている。

中性子捕捉療法

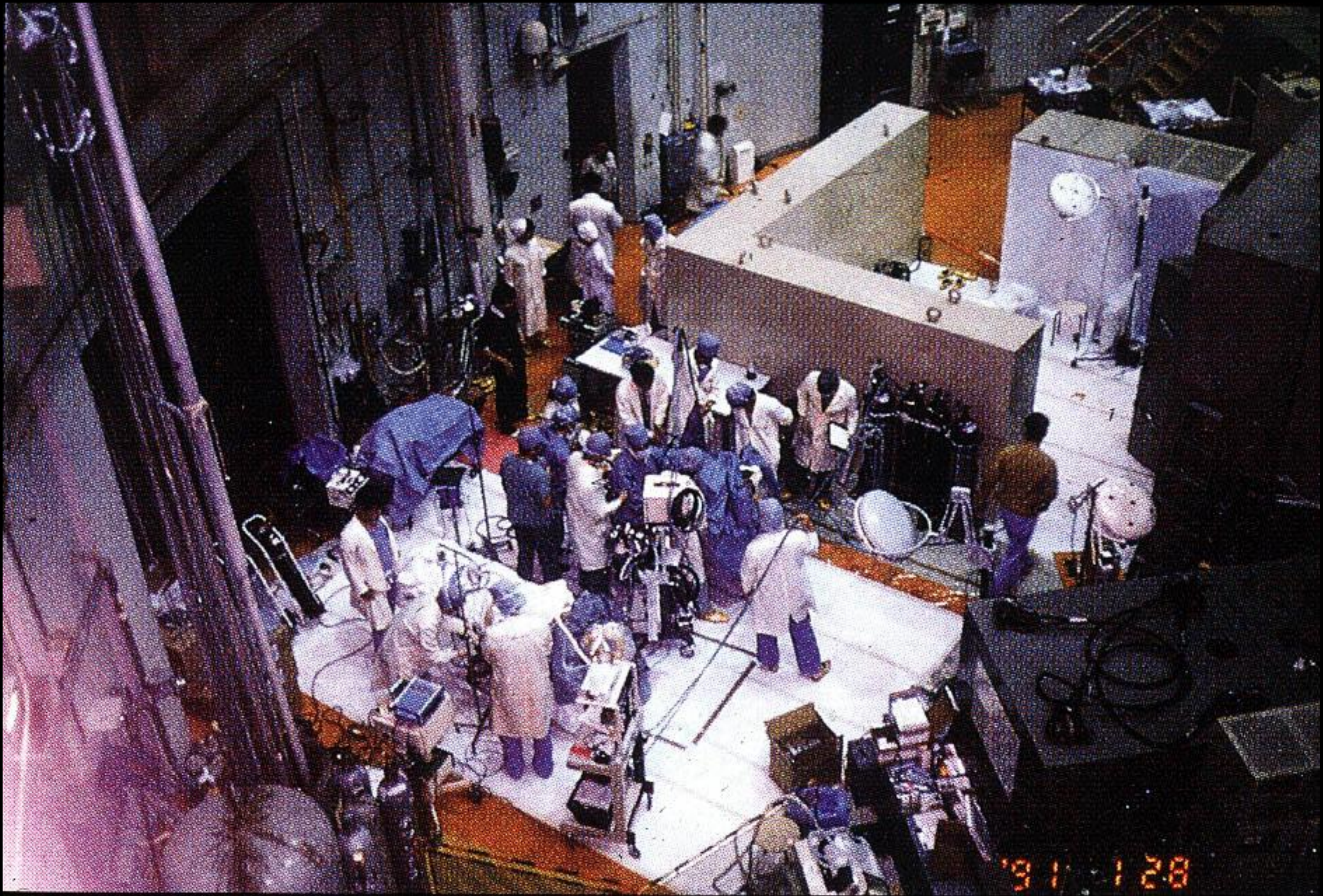


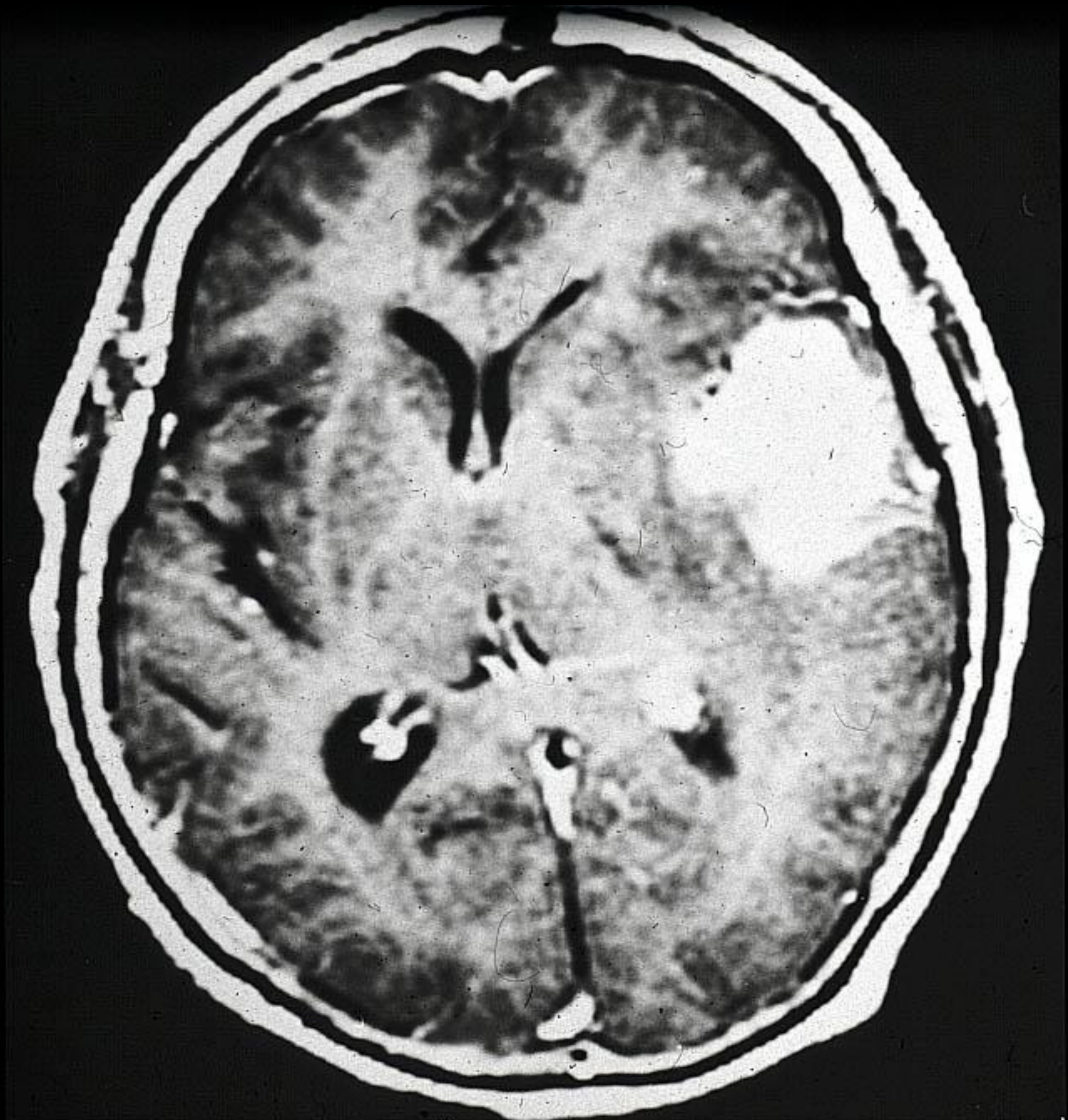
$$^{10}B + n \rightarrow {}^{7}Li + \alpha + 2.79\ \text{MeV}\ (6.1\%)$$

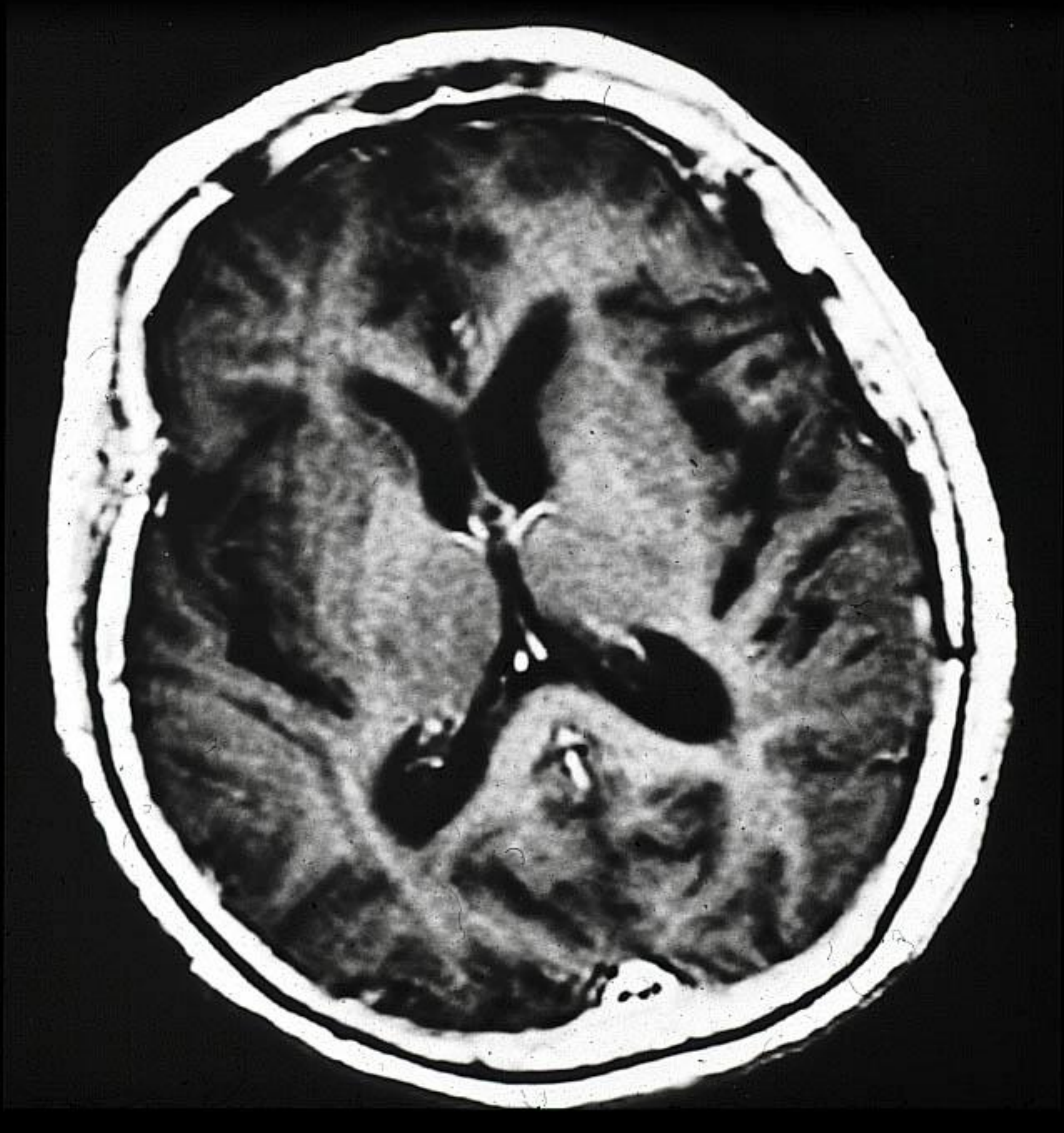
$$^{10}B + n \rightarrow {}^{7}Li + \alpha + 2.31\ \text{MeV}\ (93.9\%)$$

$$\rightarrow {}^{7}Li + \gamma + 0.48\ \text{MeV}$$

Other reactions: $^{14}N(n, p)^{4}C$, $H(n, \gamma)D$

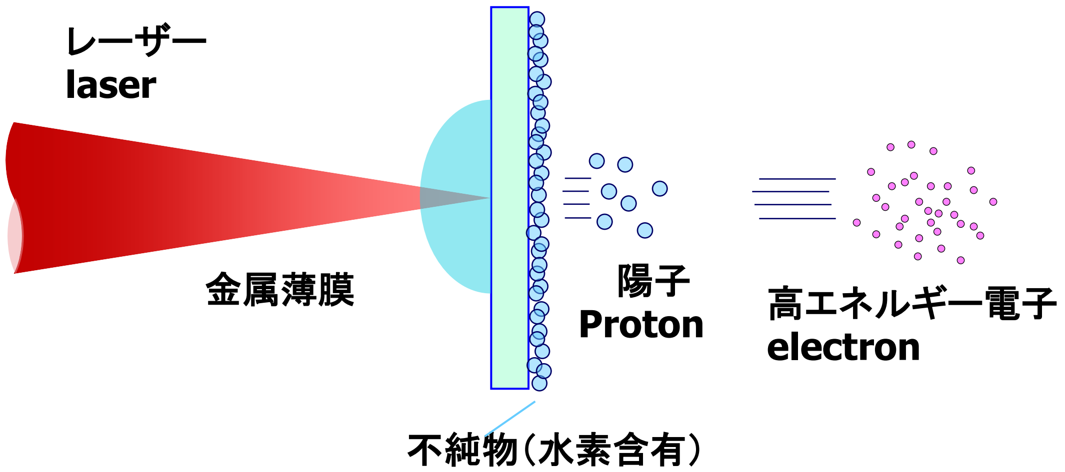

'91 1 28





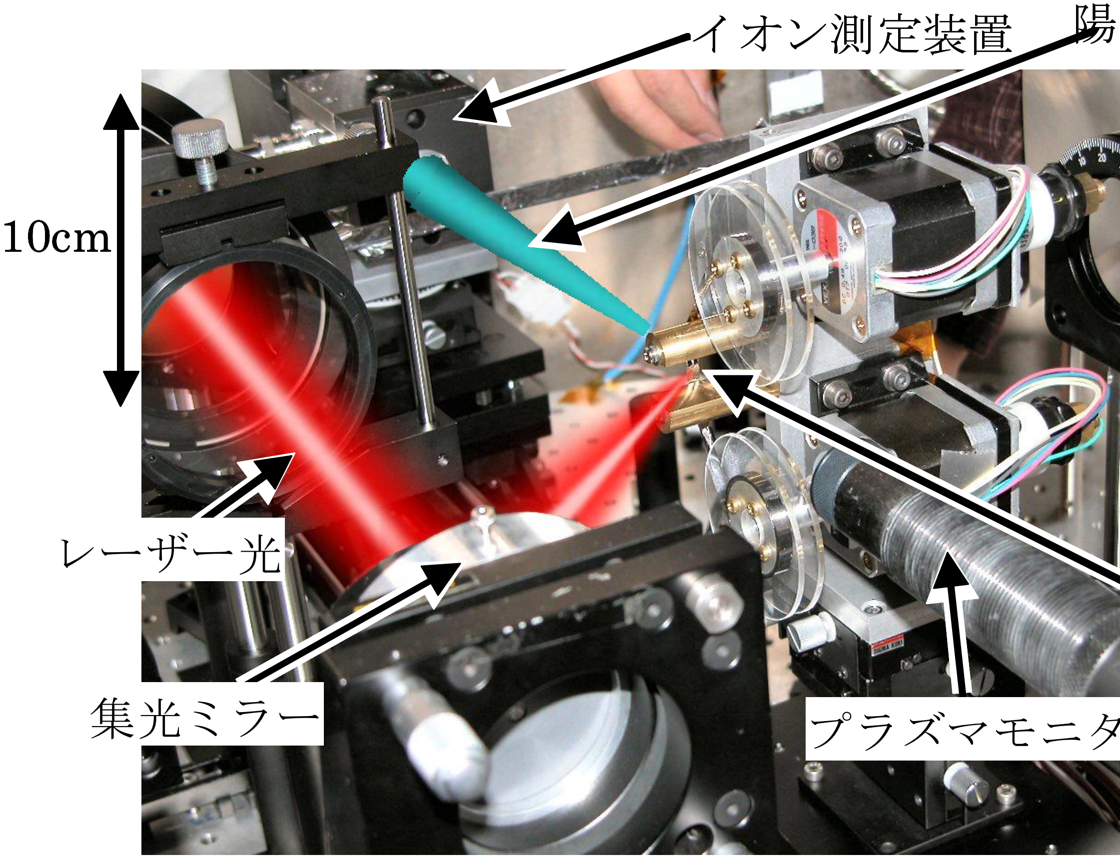
レザー駆動粒子線治療

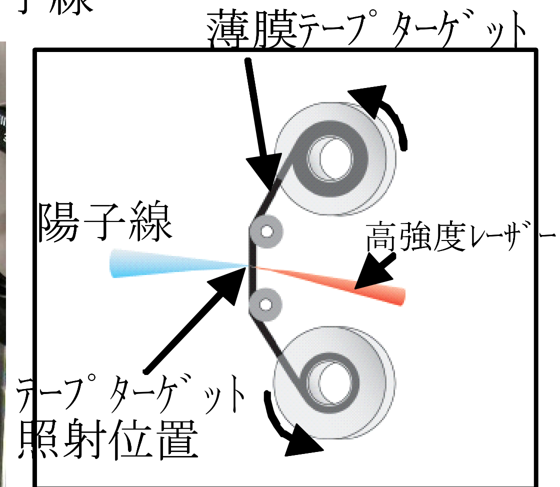
Tajima & Dawson. Physical Review Letters 43:267, 1979



レーザー駆動陽子線治療装置の特徴
Feature of laser driven proton accelerator

陽子線加速：TeV/m_





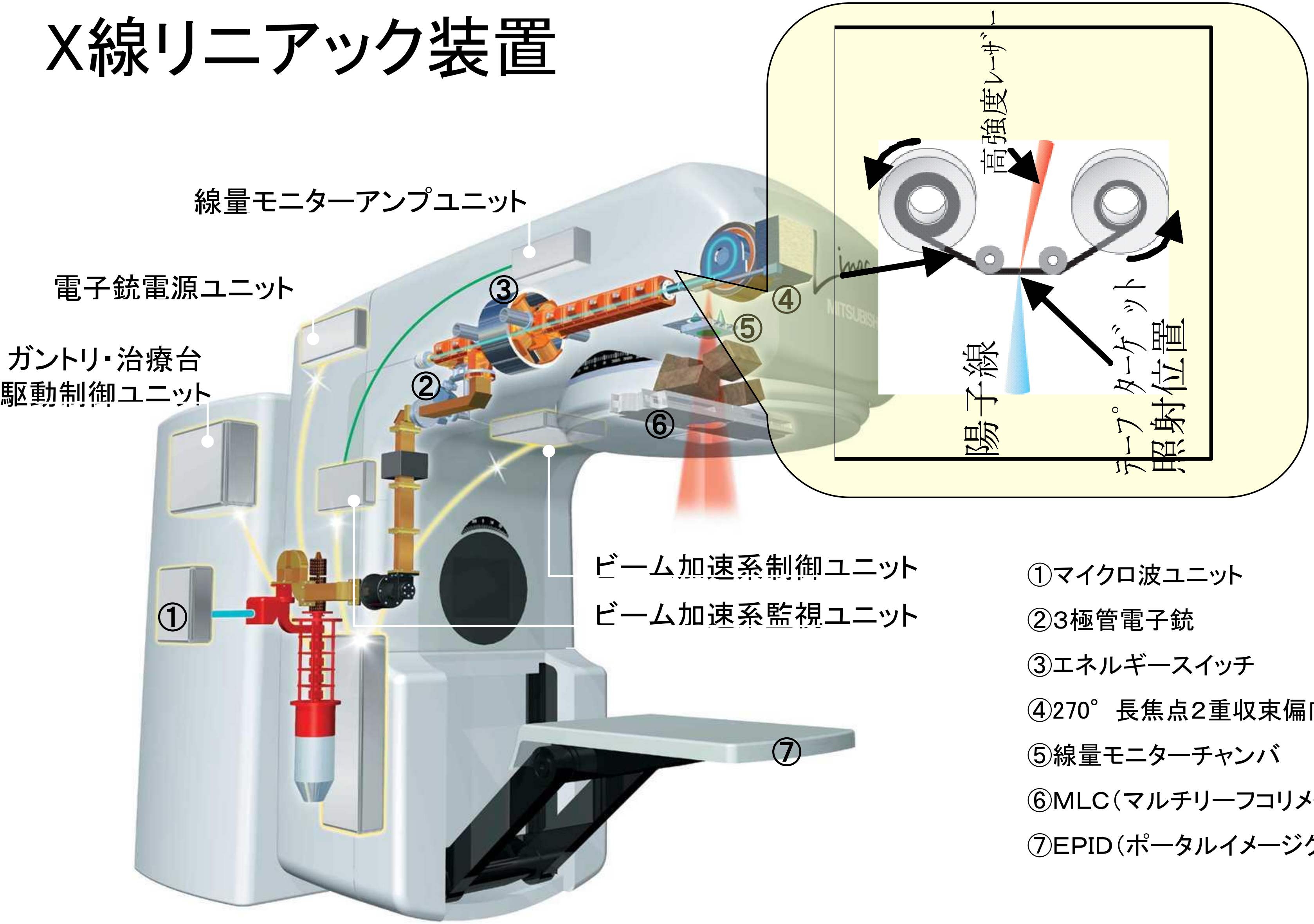
・装置が小型化できる

The device can be miniaturized.

③従来の加速器インフラへの適合

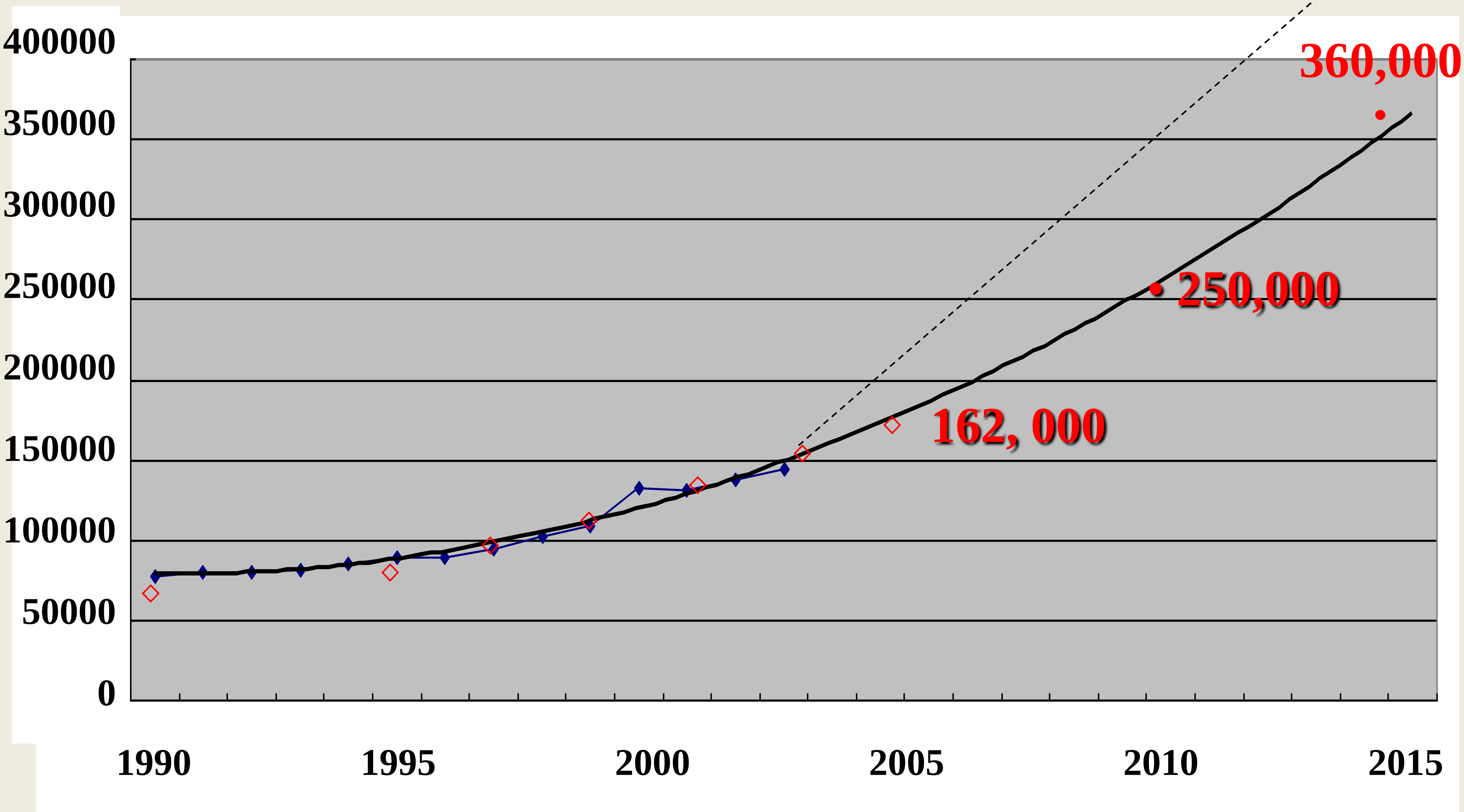
Adaptation to conventional accelerator (X-ray LINAC) infrastructure

X線リニアック装置



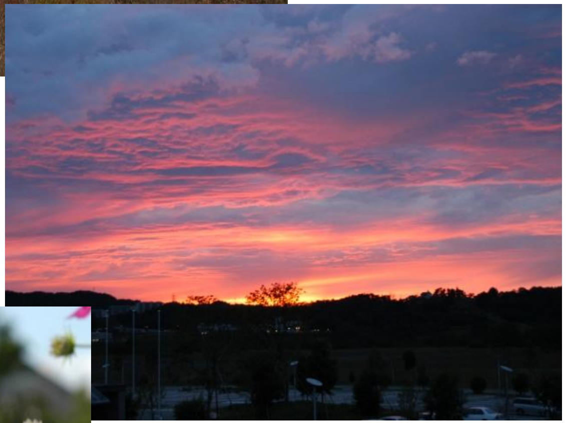
①マイクロ波ユニット
②3極管電子銃
③エネルギースイッチ
④270° 長焦点2重収束偏向システム
⑤線量モニターチャンバ
⑥MLC（マルチリーフコリメータ）
⑦EPID（ポータルイメージング装置）

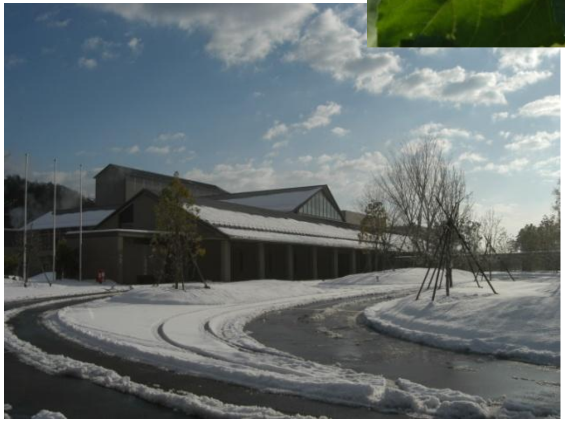
厚生労働省がん研究助成金研究班ＰＣＳ(14-6)による放射線治療新患数の予測



◇: 日本放射線腫瘍学会構造調査

JPCS WG





Thank you for your kind attention.

Hyogo Ion Beam Medical Center