

Introduction à la radiothérapie

UE 19 - item 294 / 291

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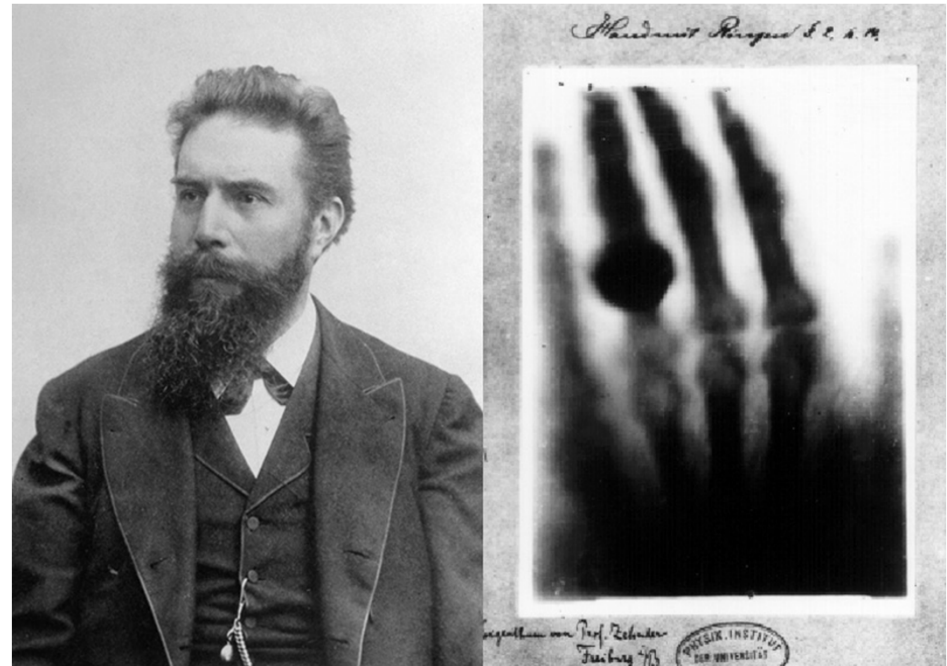


Introduction

Les Rayons X

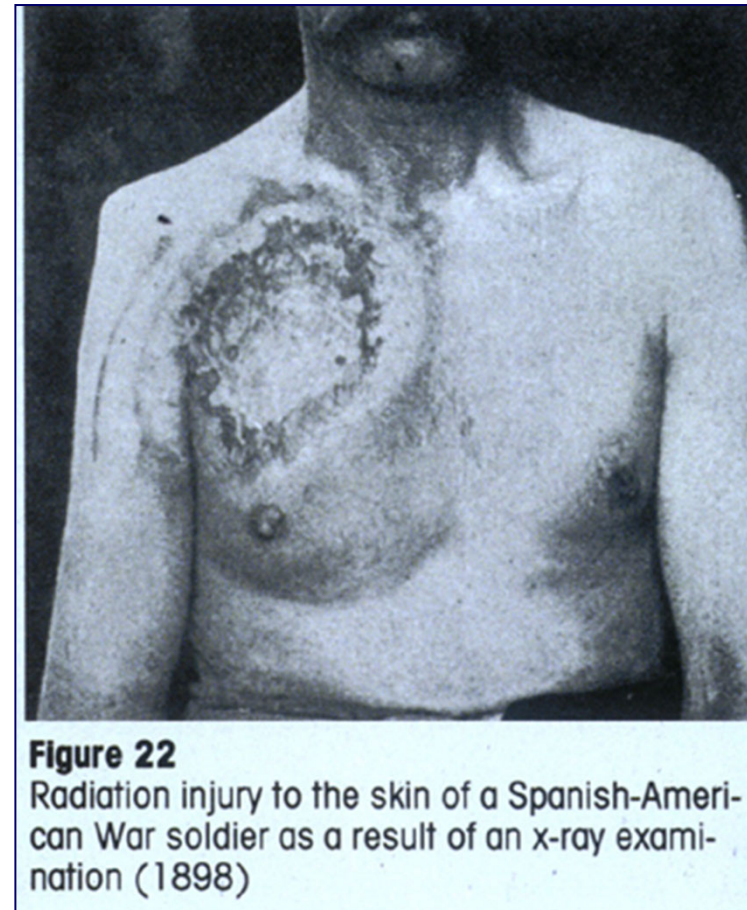
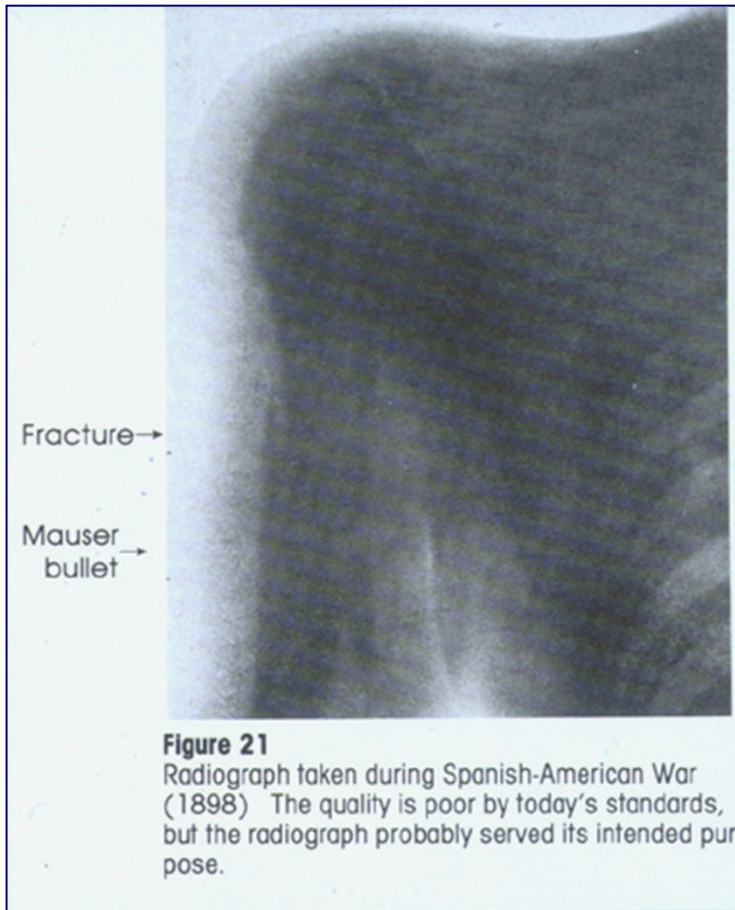
Découverte des Rayons X par Conrad Roentgen fin 1895.

Utilisés à toutes sortes de fins, médicales et non médicales, de nombreux accidents sont rapportés dès 1896, puis des cancers de la peau un peu plus tard.



1845-1923

Une des premières radiographies...

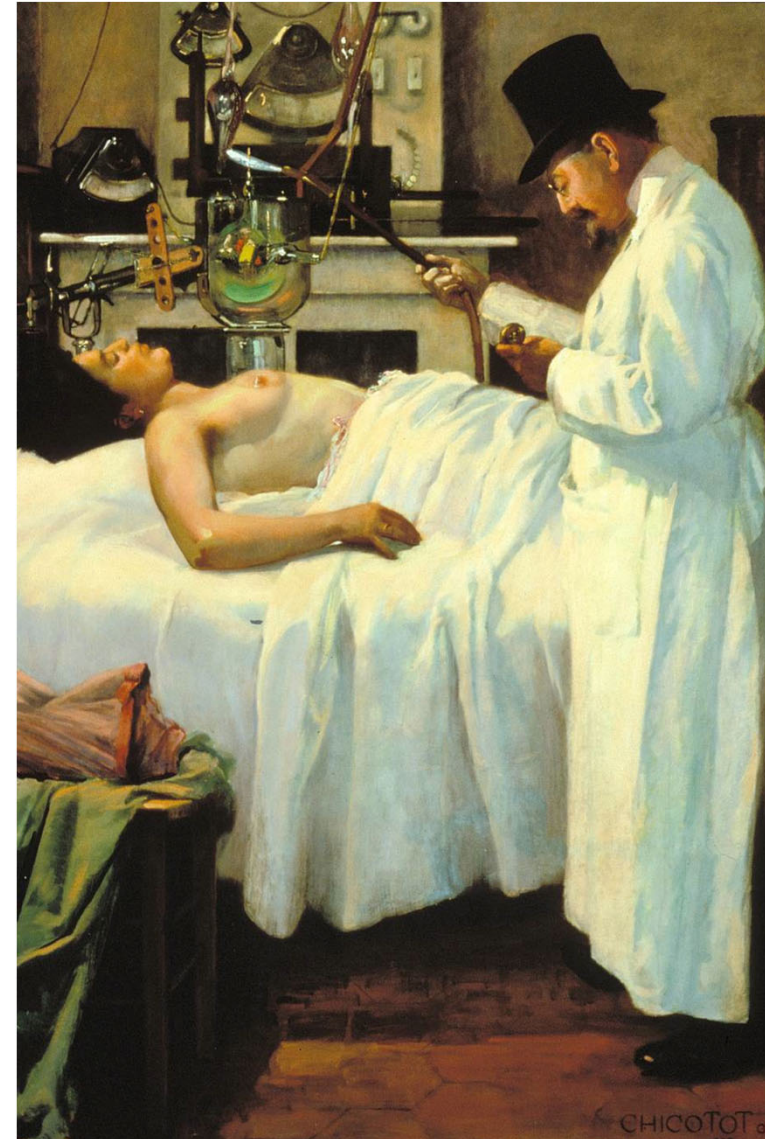


Rayons X

Découverts en 1895 et
immédiatement appliqués au
traitement du cancer.

Pourquoi?

Parce que la chirurgie était la
seule option, et elle était
dangereuse...



C

Utilisation thérapeutique des Rayons-X



Et à Lyon...?

1^{er} traitement par Rx en
1896 pour un lymphome (?)
gastrique

Victor Despeignes (1866 - 1937)

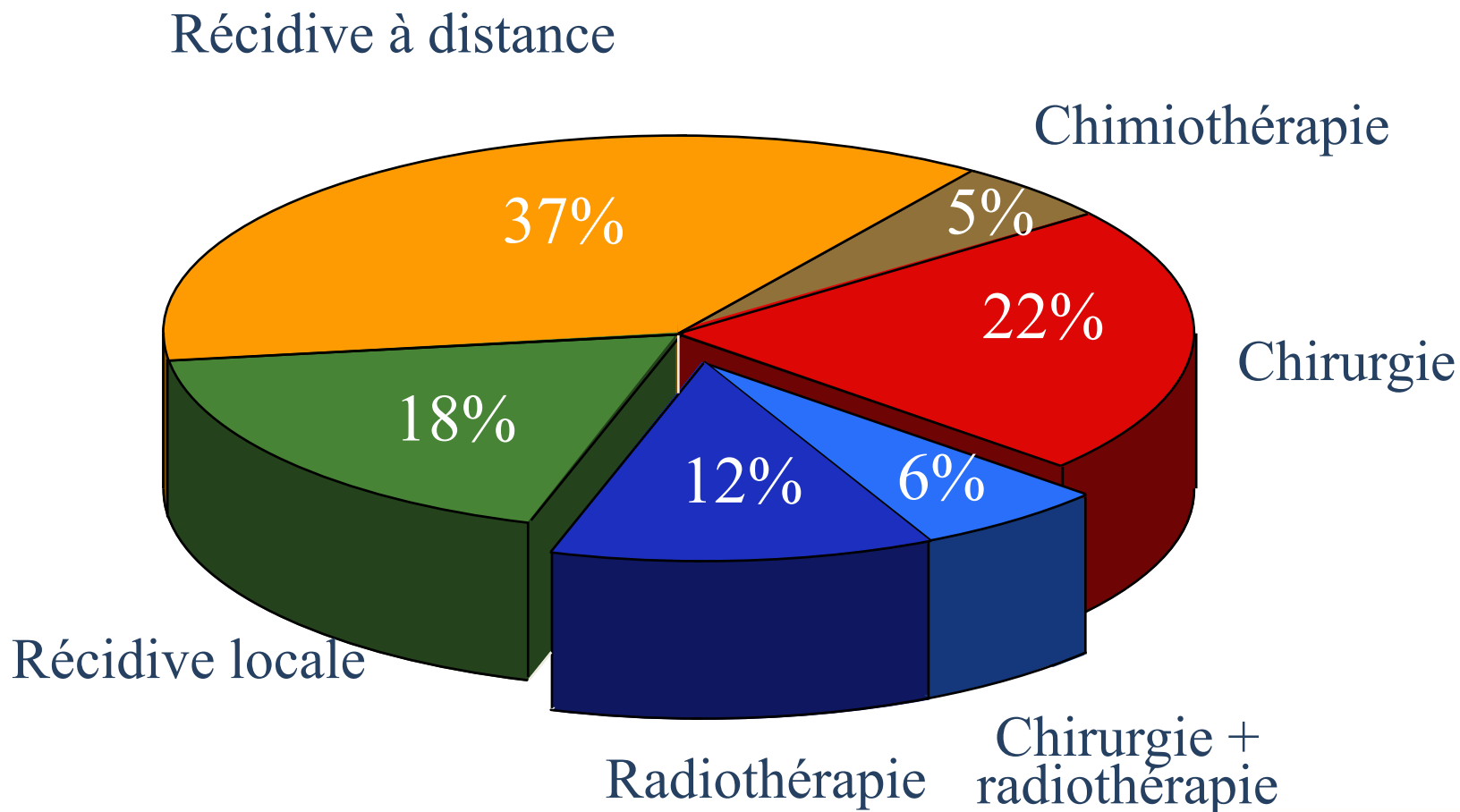
A

La radiothérapie en 2019 en quelques chiffres

- 433.136 nouveaux cas estimés de cancer en 2023 en France métropolitaine
- 46.000 cancers en région Auvergnnes-Rhône-Alpes
- 50-60% bénéficieront d'un traitement par radiothérapie à visée curative ou palliative

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Faits et mythes en oncologie



Types of ionizing radiation

- Electromagnetic radiation (low LET): photons, g-rays, X-rays
- Particulate Radiation (high LET)
 - charged particles: electrons, protons, α particles
 - neutrons
 - heavy charged ions: carbon, neons, argon, ...

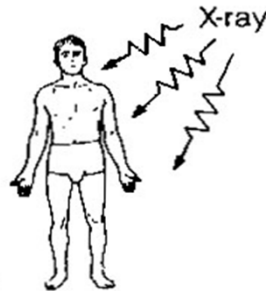
Quantities and units

Absorbed dose: 1 Gray (Gy) = 1 joule/kg
 = increase of 0.0001 °C per gr
 water

Total-Body Irradiation

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

$$\begin{aligned} 70 \times 4 &= 280 \text{ joules} \\ &= \frac{280}{4.18} = 67 \text{ calories} \end{aligned}$$



Drinking Hot Coffee

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

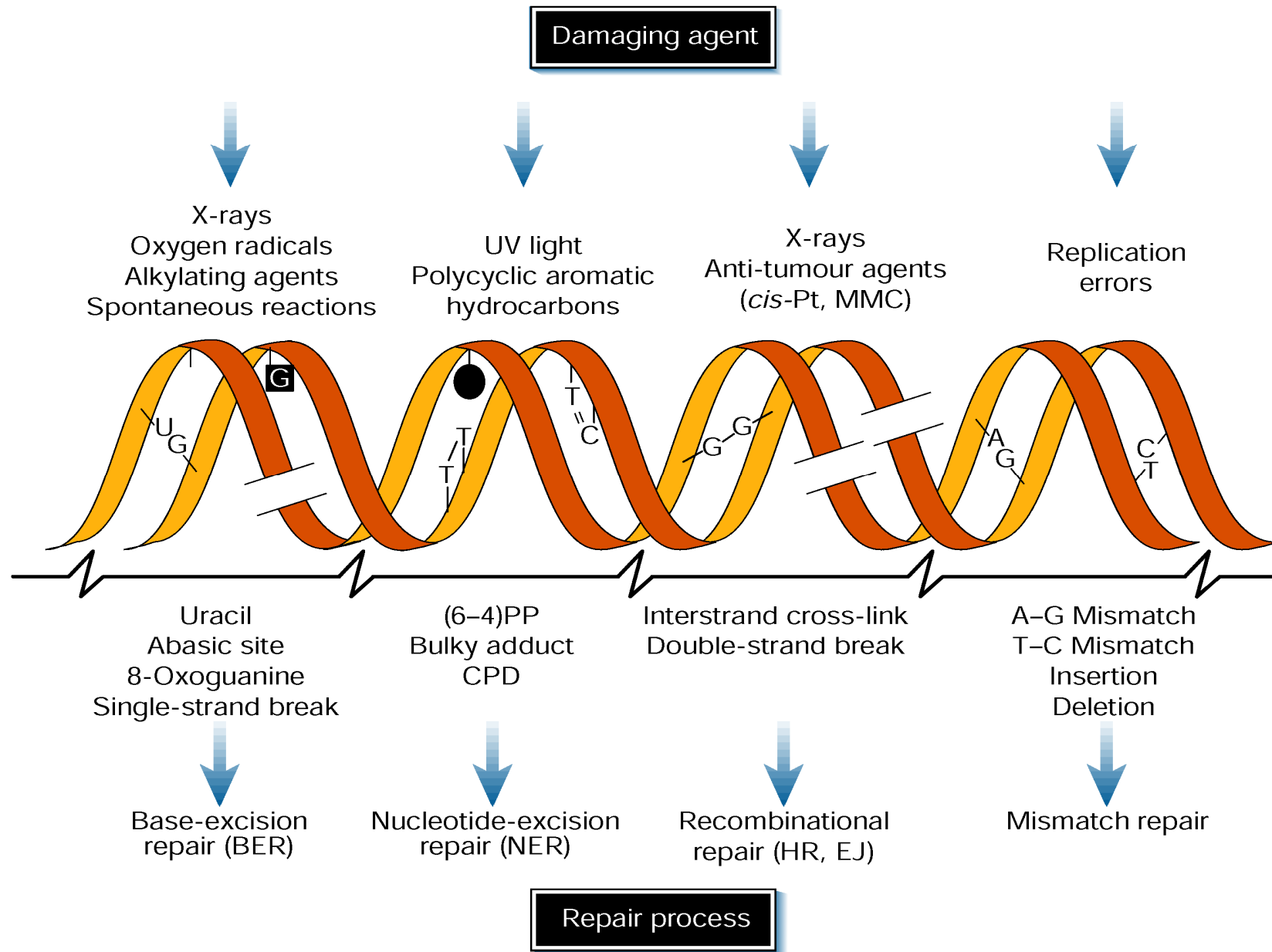


$$\begin{aligned} &= 3 \text{ mL} \\ &= 1 \text{ sip} \end{aligned}$$



Biological bases of radiotherapy

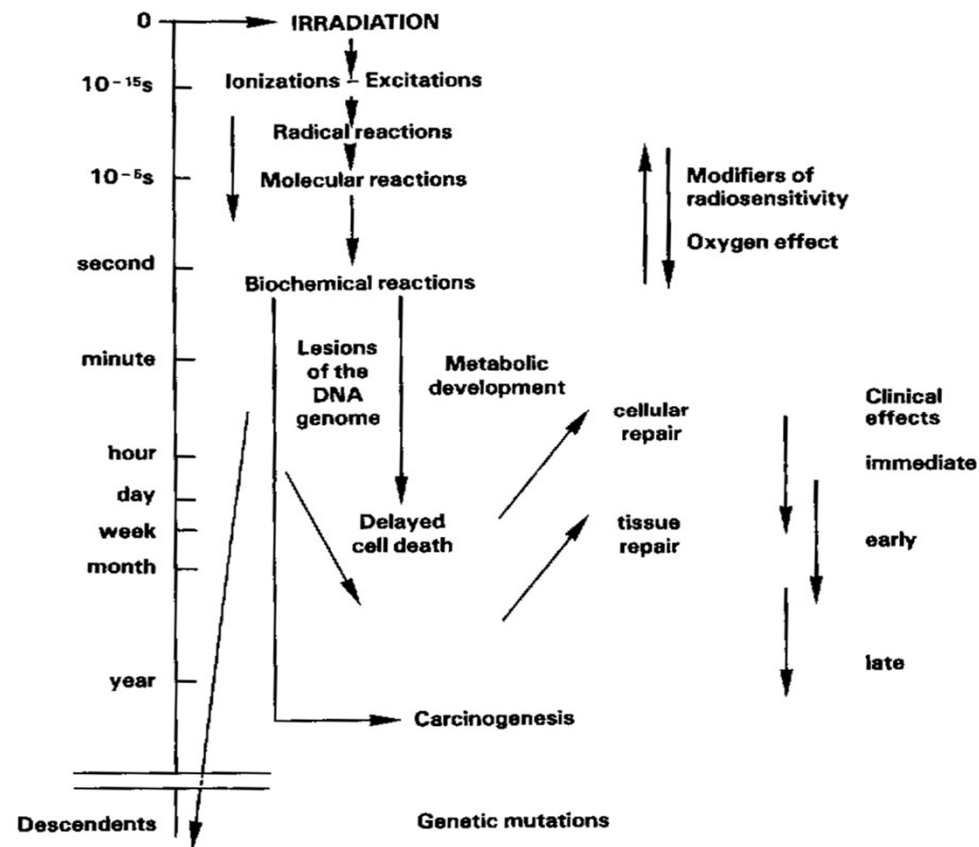
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B

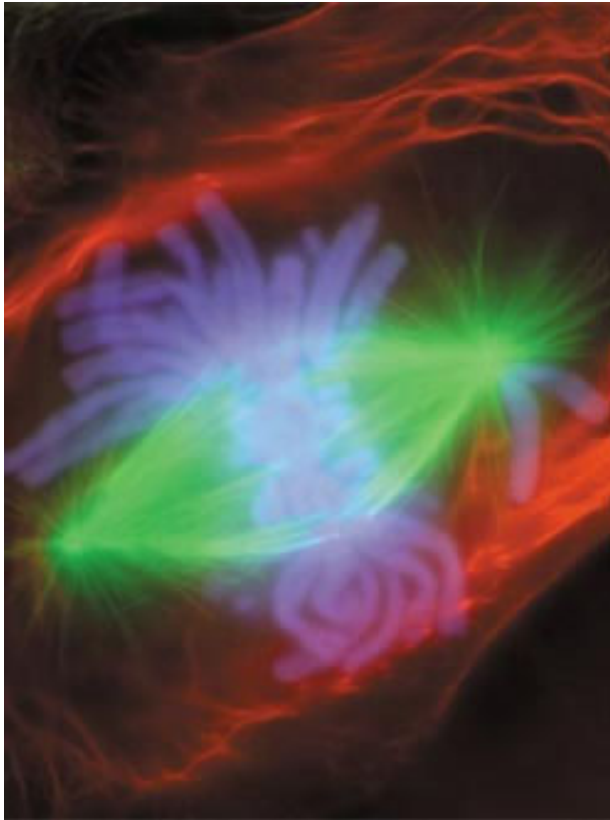
The physics and chemistry of radiation absorption

Chronology of events



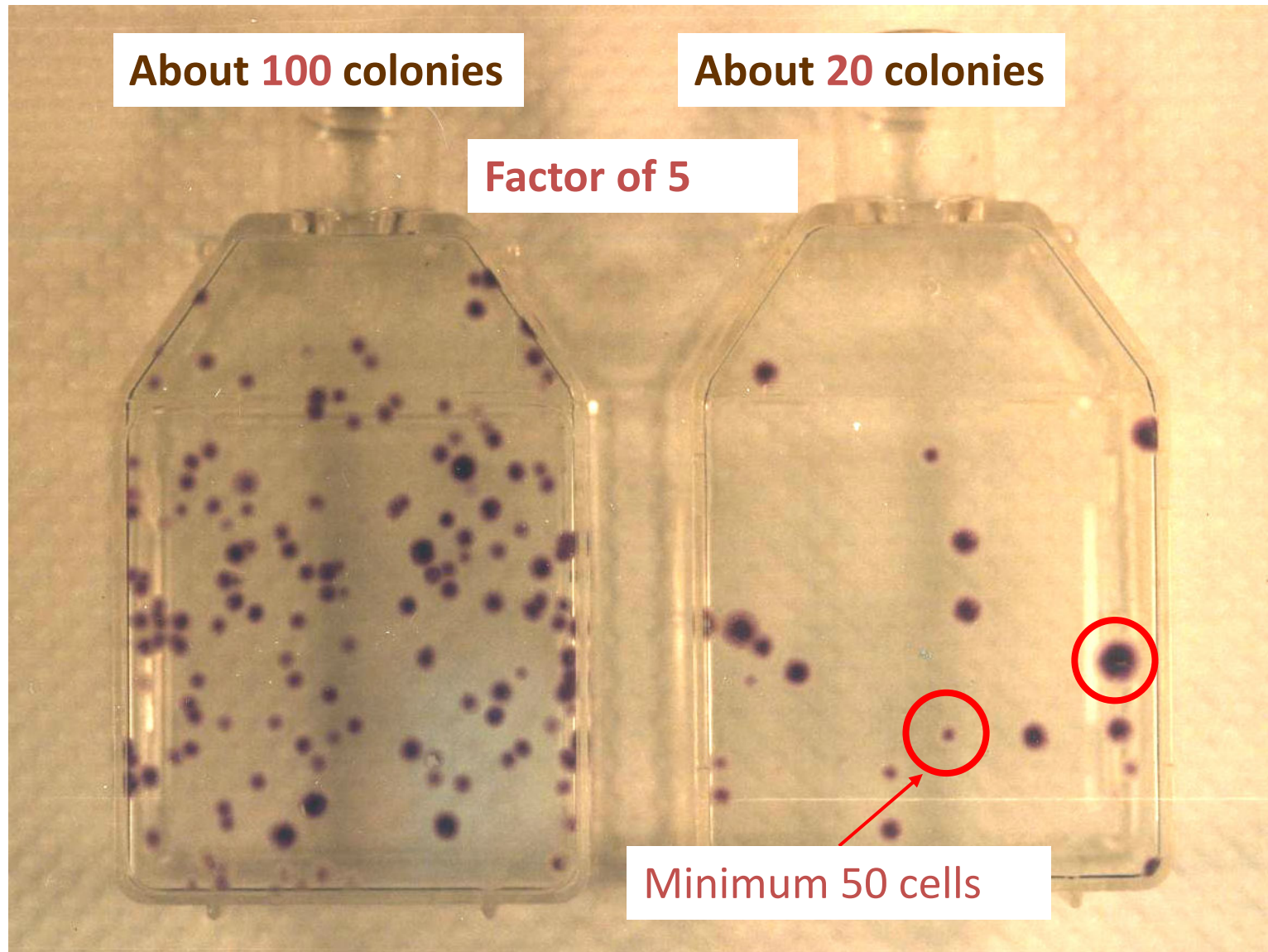
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Effects of irradiation on mitosis



Effects on mitosis in plant cells:
endosperm of Haemanthus - time-lapse movie A. Bajer (1962)

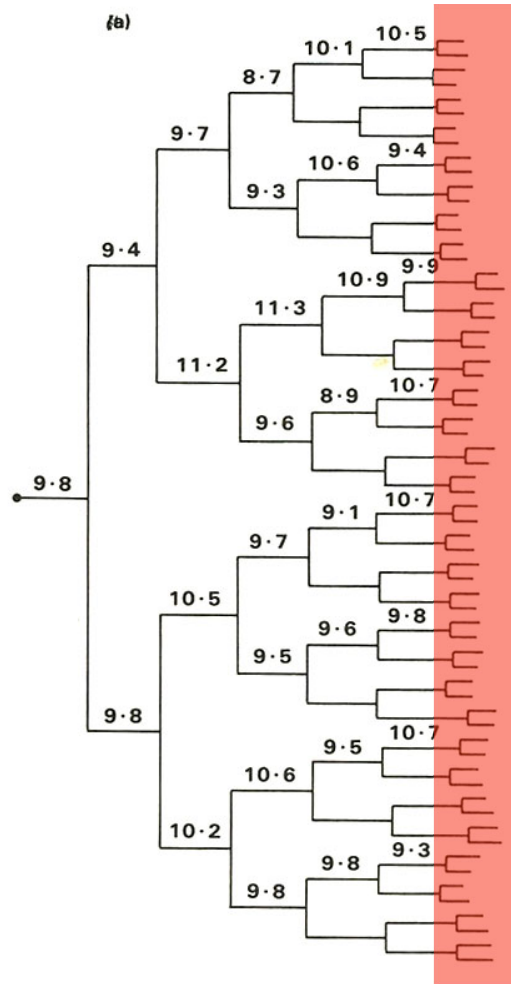
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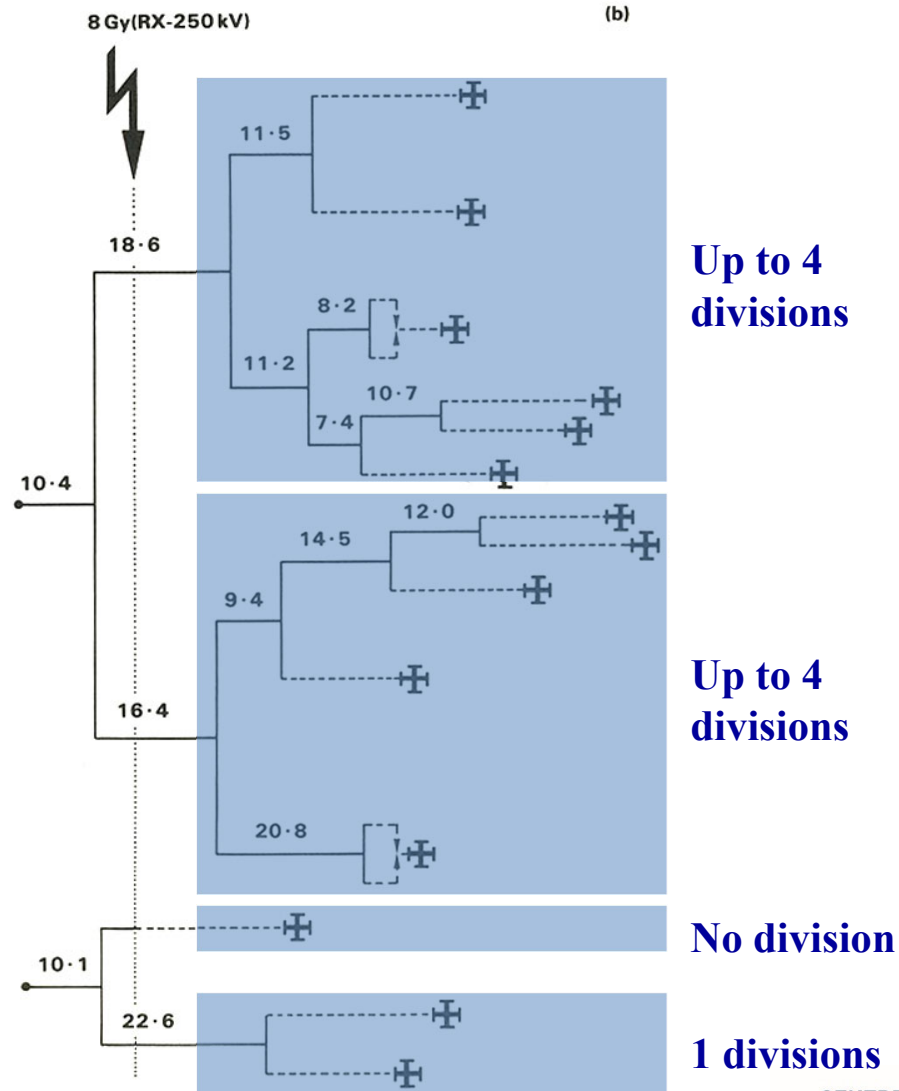
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Unirradiated cells

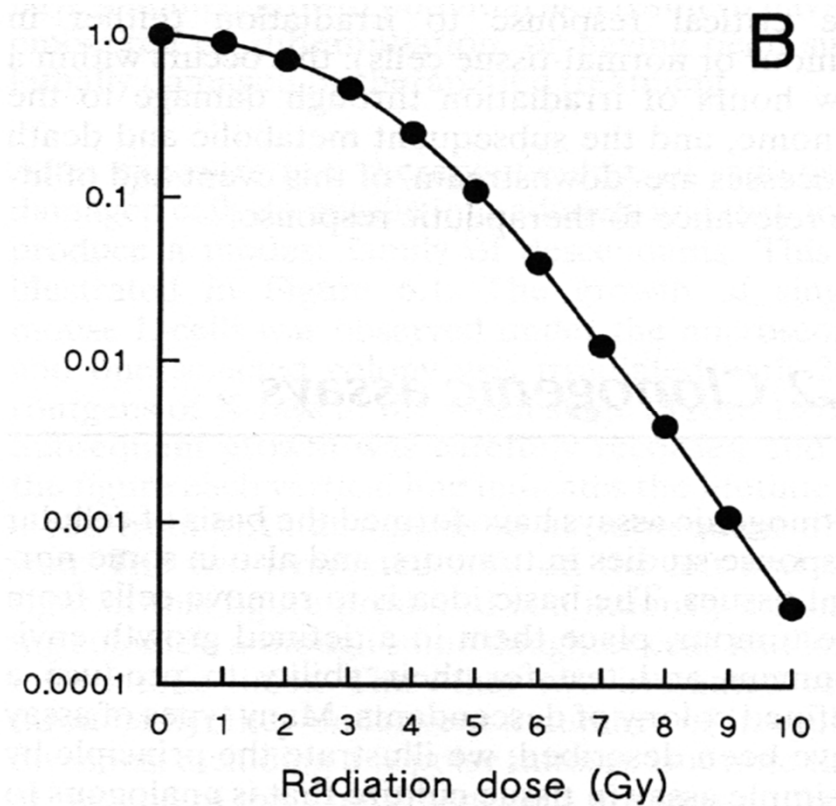
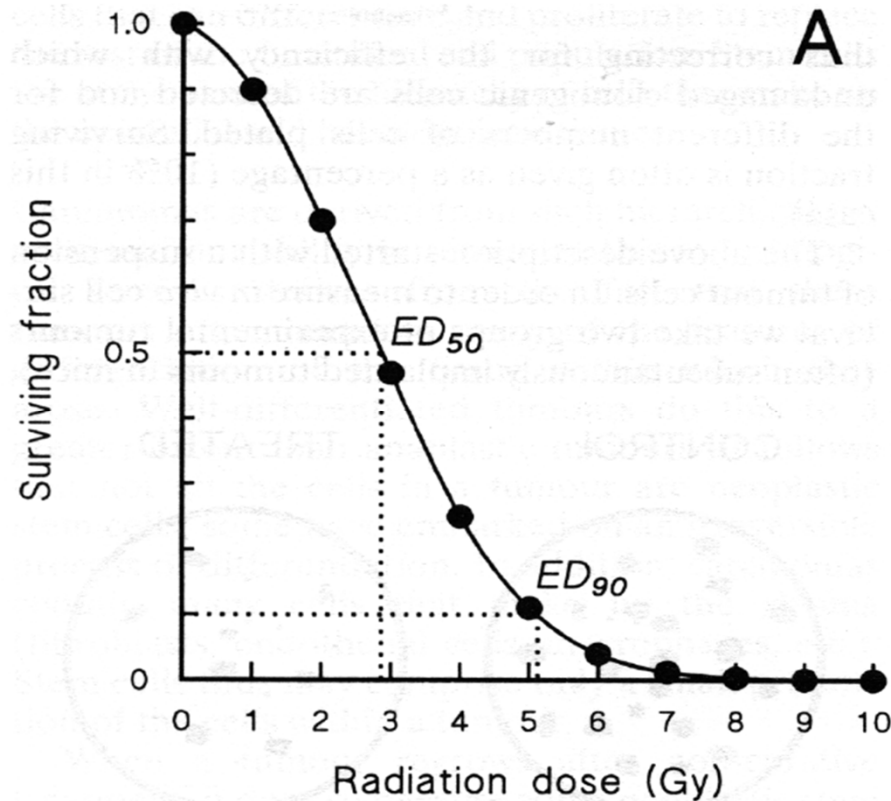


Irradiated cells



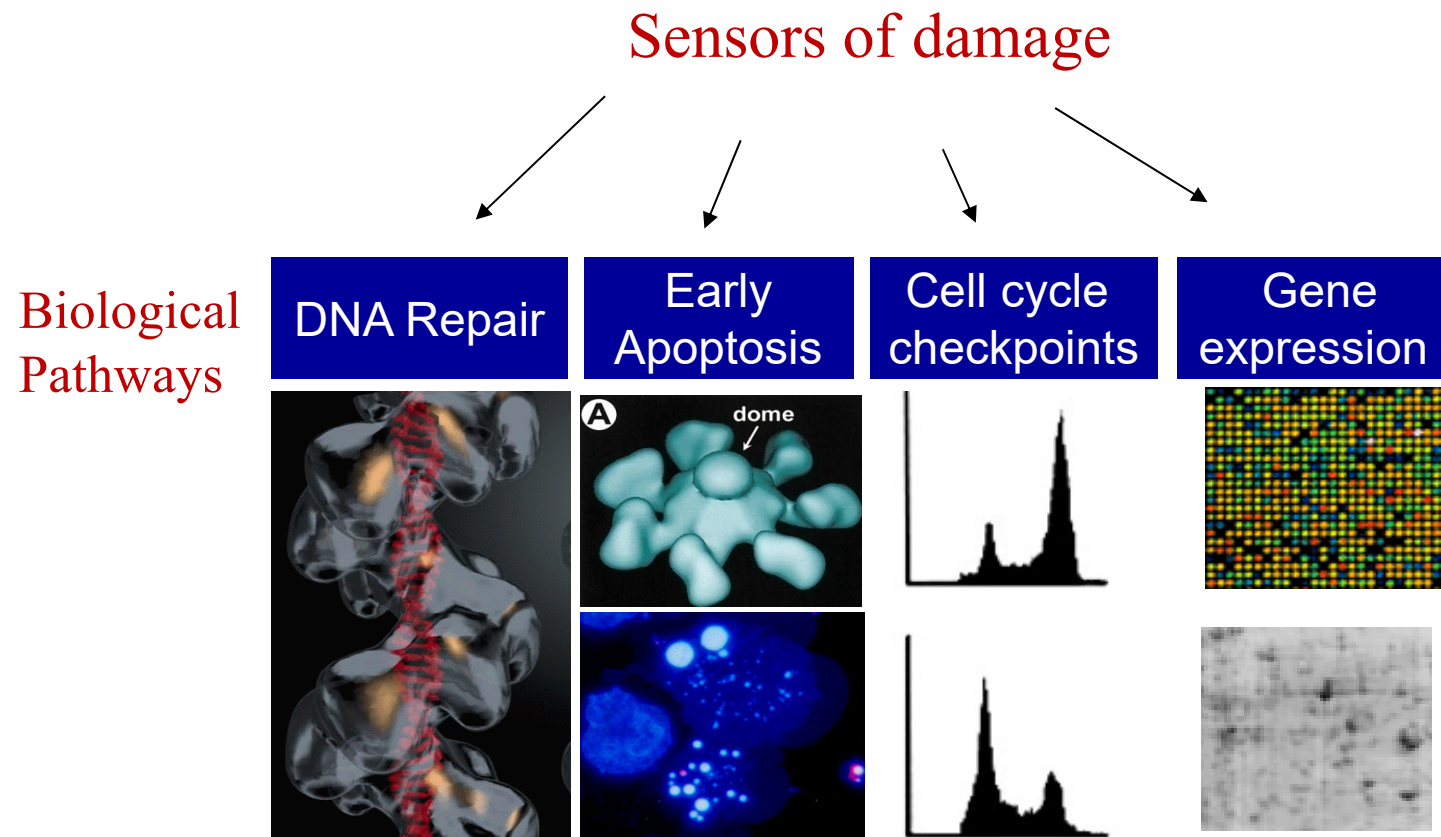
B

Cell survival curves



B

Initial cellular responses to radiation

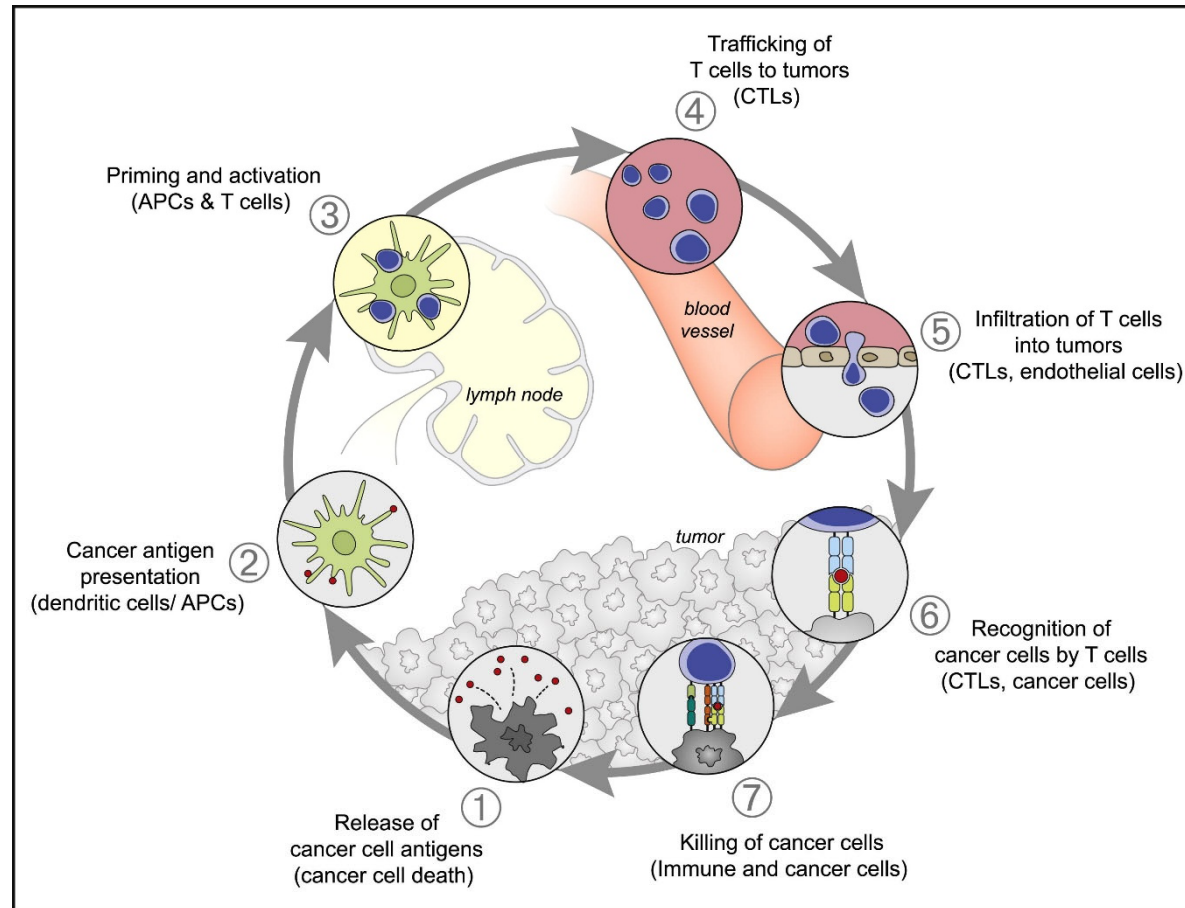


HR and Human Disease

Many diseases associated with the sensors and transducers

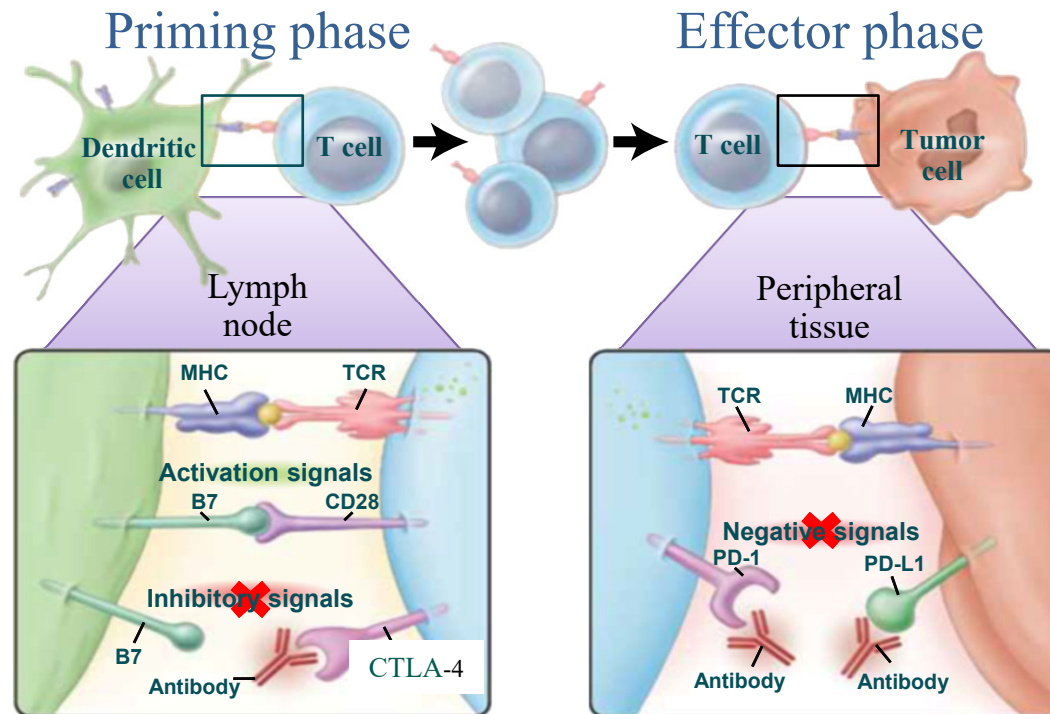
- Ataxia Telangiectasia – mutations in ATM
 - Patients are radiosensitive
 - Elevated risk of cancer
 - Have several developmental and neural abnormalities
- AT like disorder – mutations in MRE11
- Nijmegen breakage syndrome – mutations in NBS
- Familial (inherited) breast cancer - BRCA1, BRCA2
 - Inherited breast and ovarian cancer
- Fanconi's Anemia – FANCA,B,C,D1,D2,E
 - FANCB,D1=BRCA2
 - Sensitive to crosslinking agents
 - Increased risk of cancer

Immune modulation



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The role of immune checkpoint pathways in the immune response



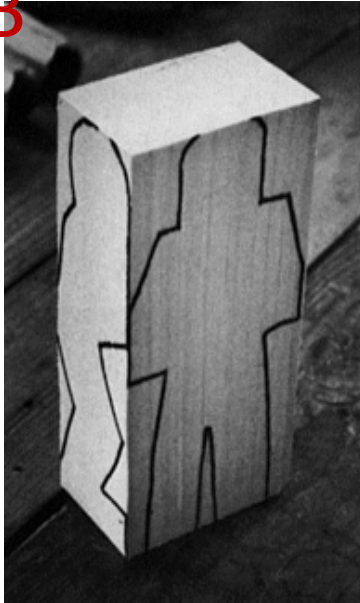


Technological aspects of radiotherapy and their evolution

B

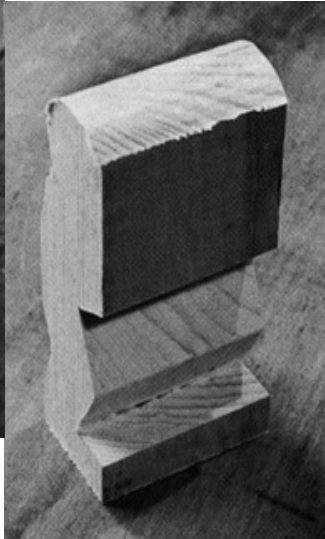
Son évolution...

2-D Planning

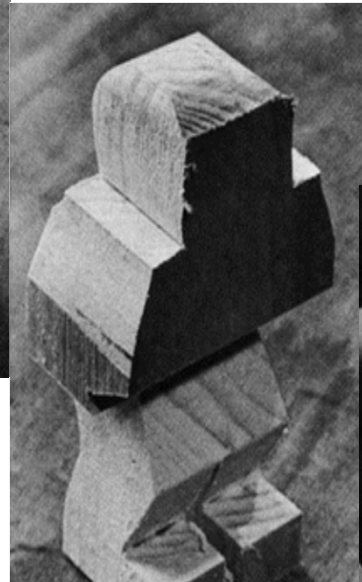


< 1950

3-D
Conformal



≈ 1960



≈ 1990

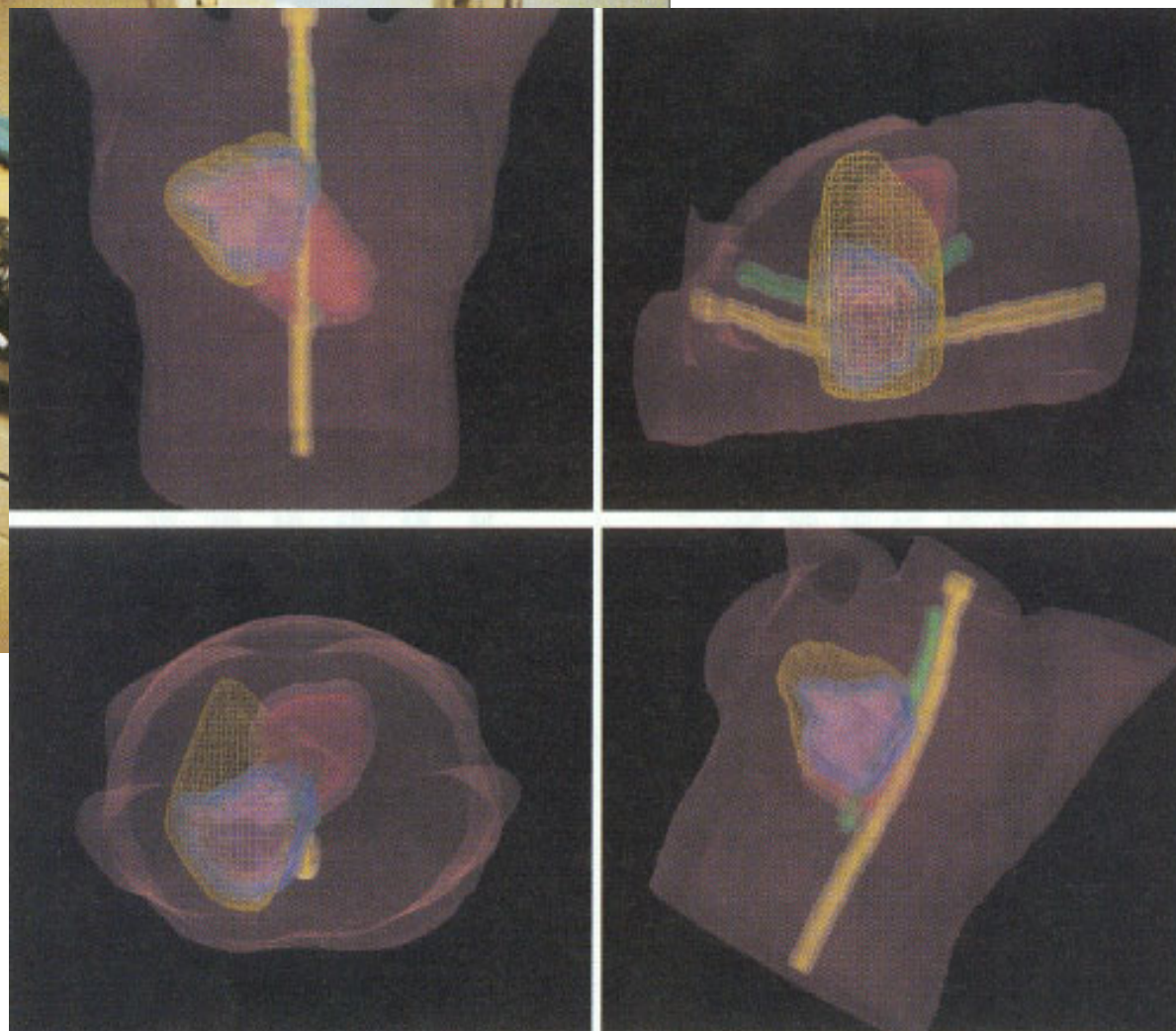
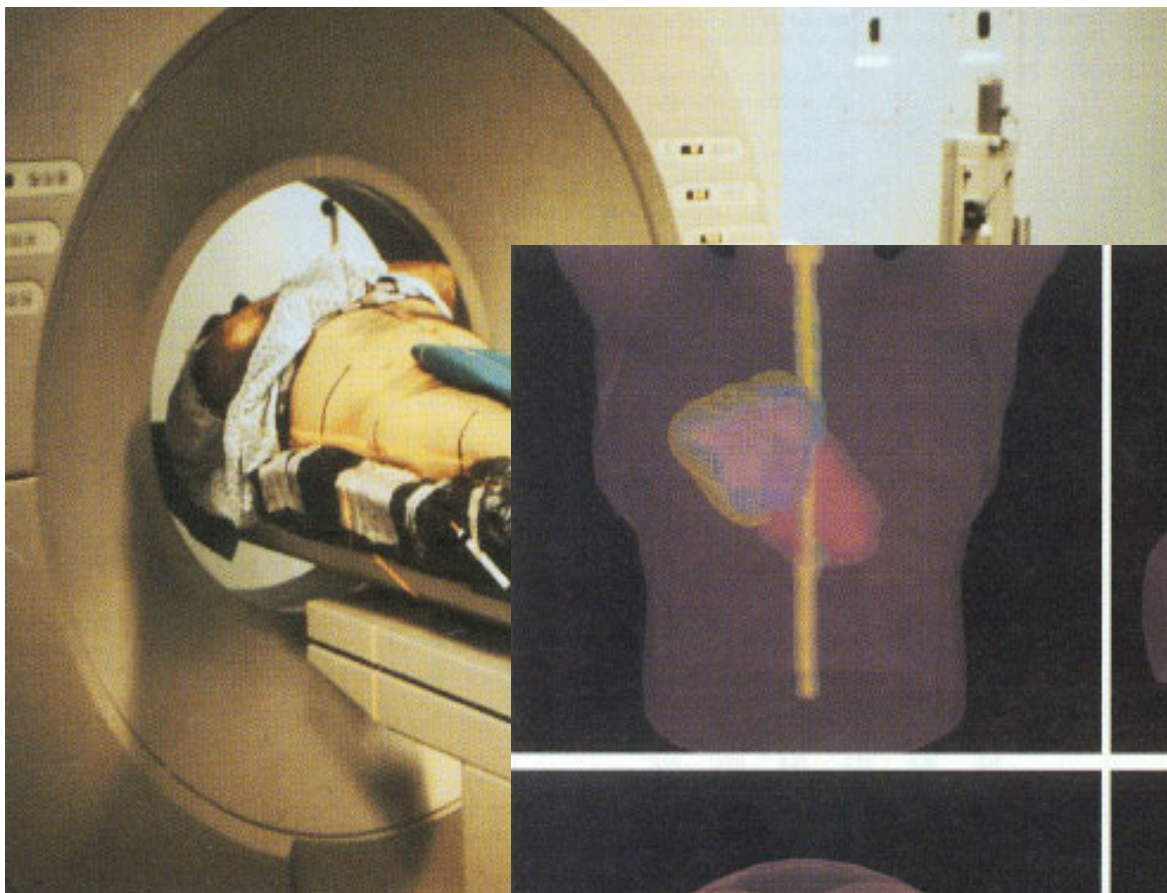
IMRT



≈ 2000

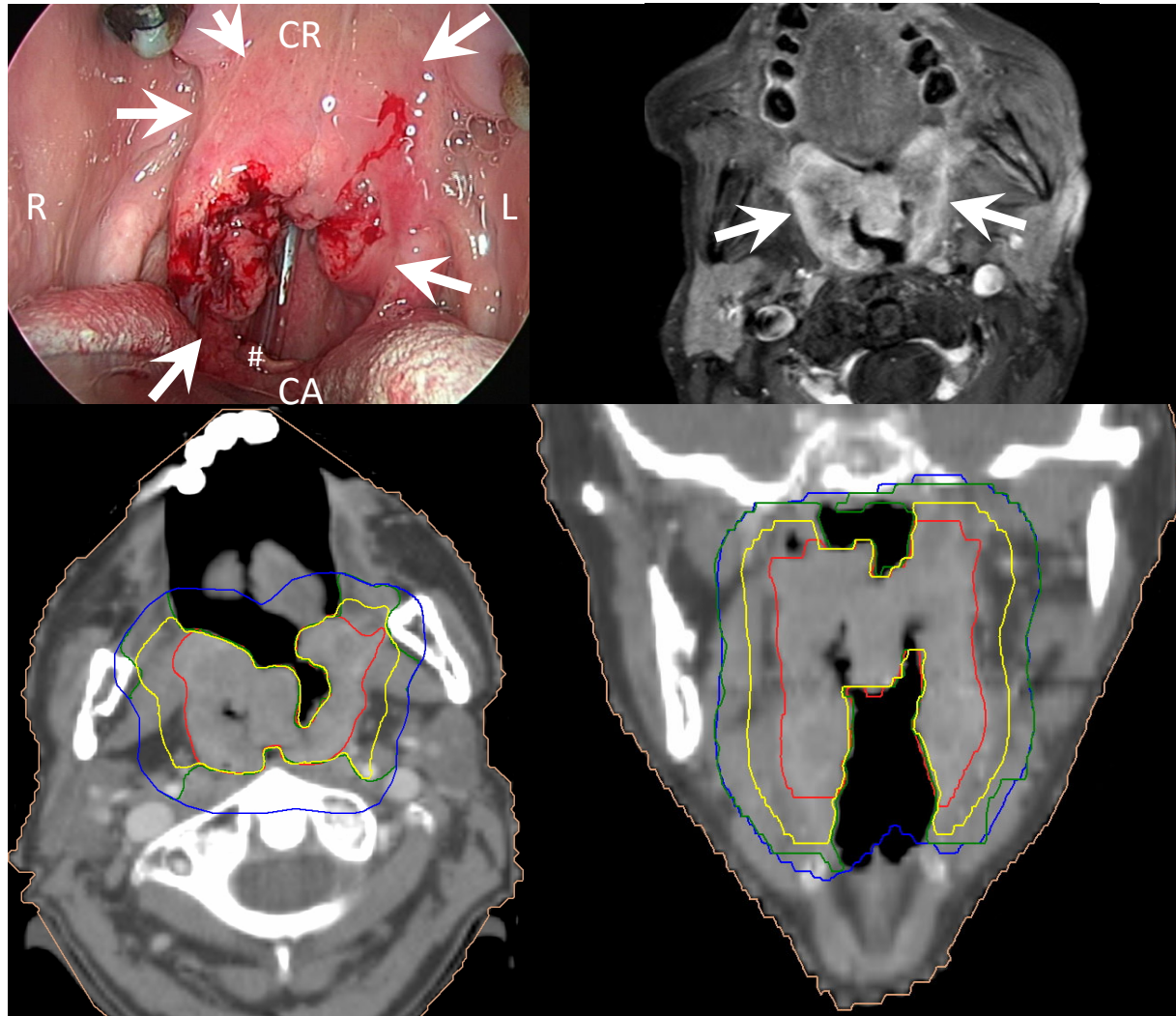
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C

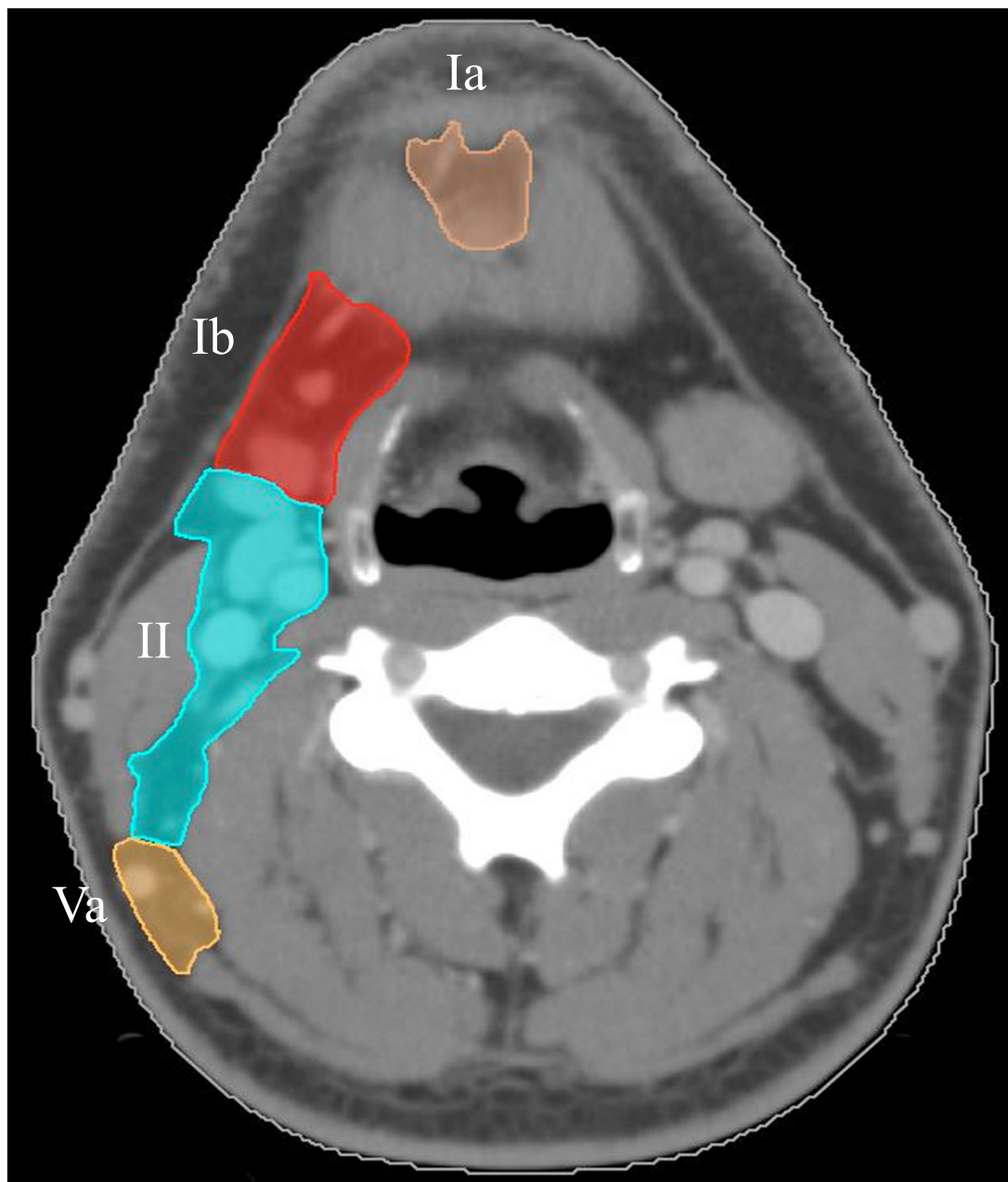
From GTV_p to CTV_p delineation T3 soft palate SCC



Edited for:

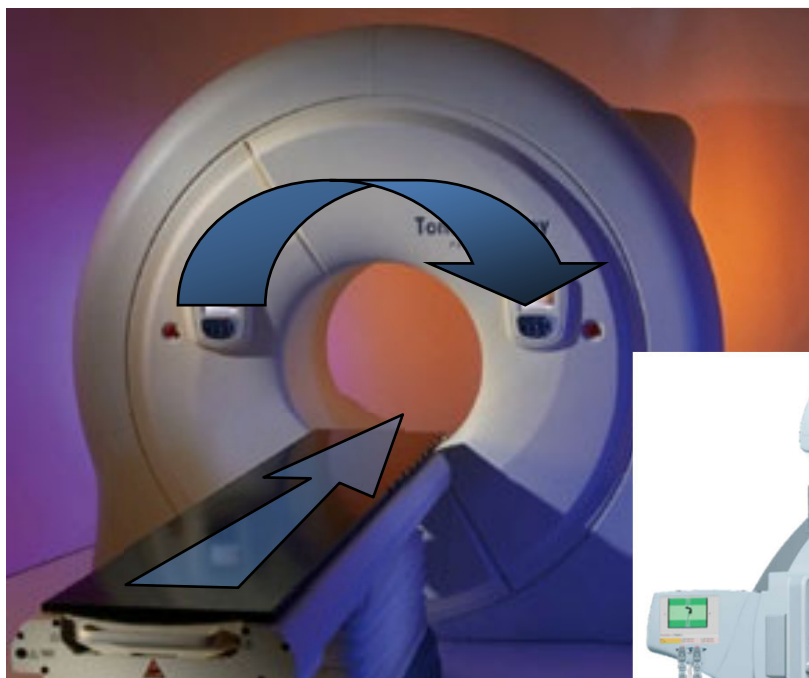
- air cavities
- mobile tongue
- mandible
- vertebral body
- longus colli & longus capiti m.
- epiglottis
- hyoid bone

C

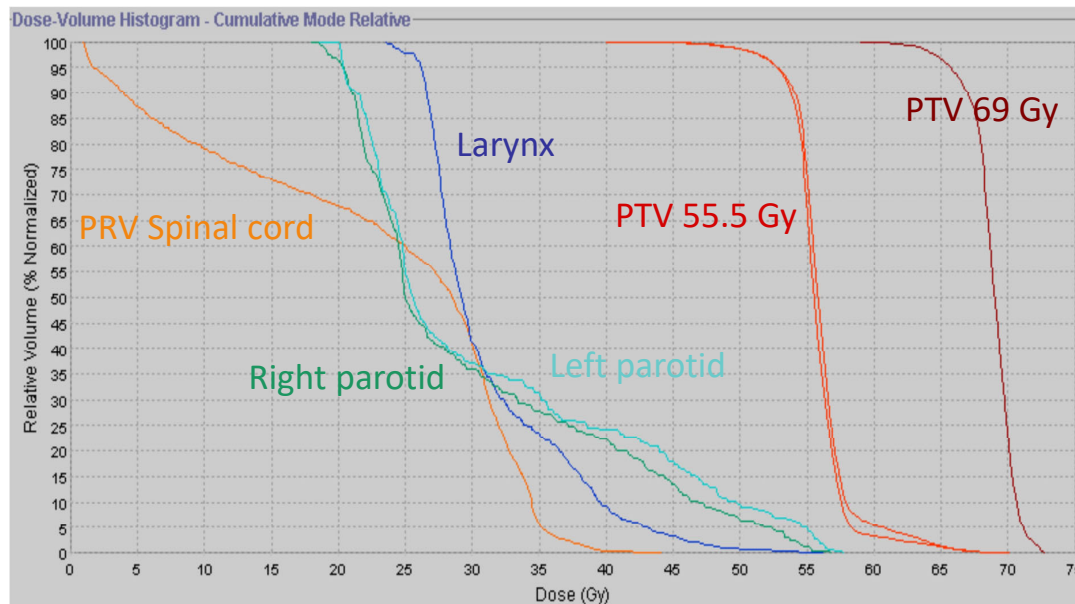
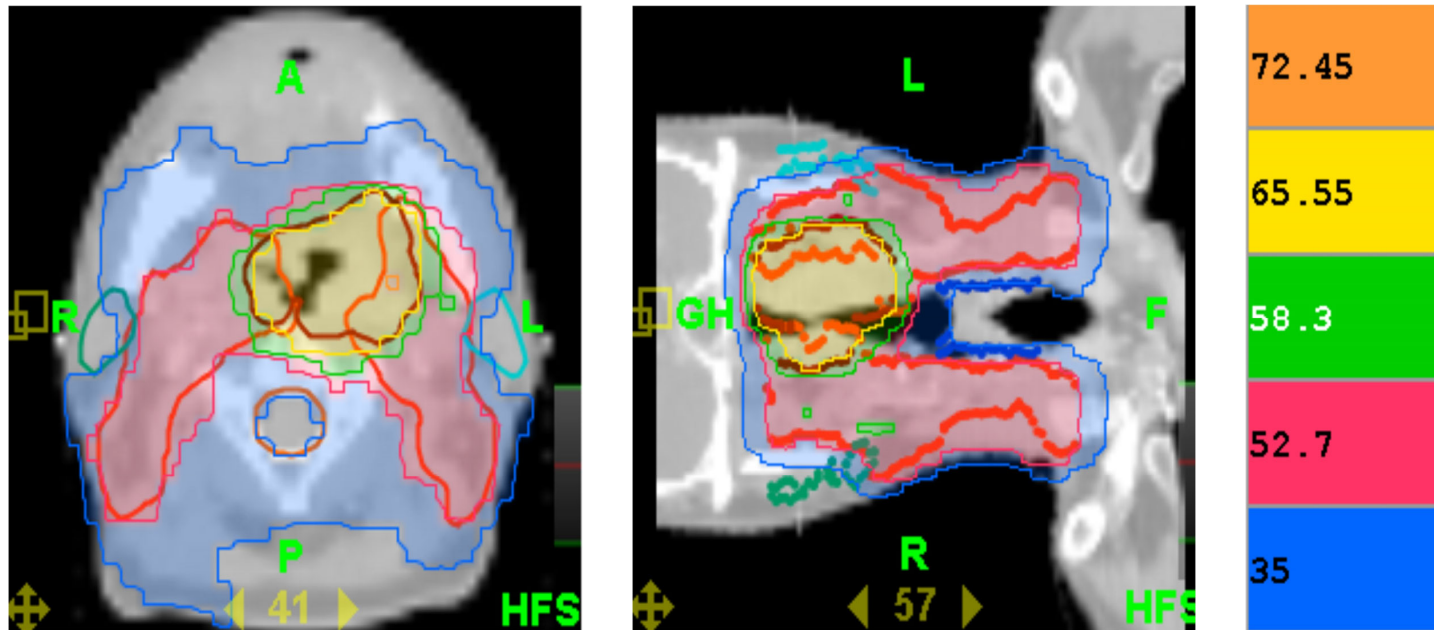


B

Différents appareils produisant des rayons-X



AIMRT/VMAT dans les tumeurs Tête & Cou



Oropharyngeal SCC

T2-N0-M0

SIB-IMRT: 30x2.3 Gy

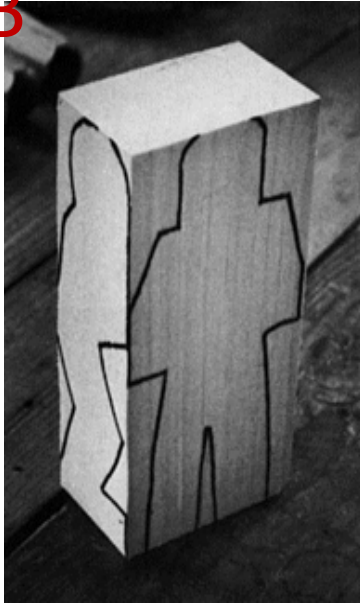
30x1.85 Gy

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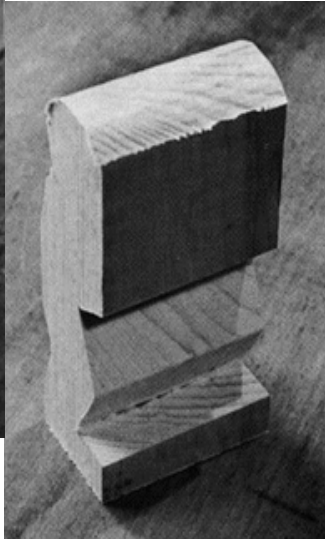
Son évolution...

2-D Planning



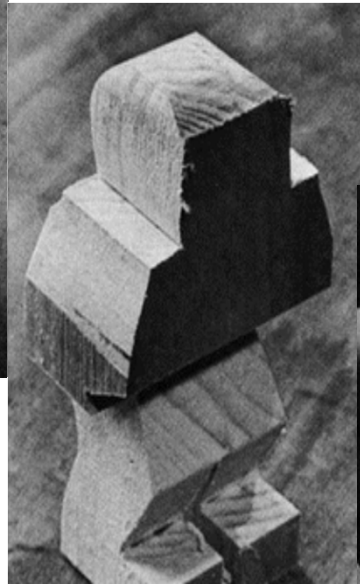
< 1950

3-D
Conformal



≈ 1960

IMRT



≈ 1990

Dose
Painting



≈ 2000



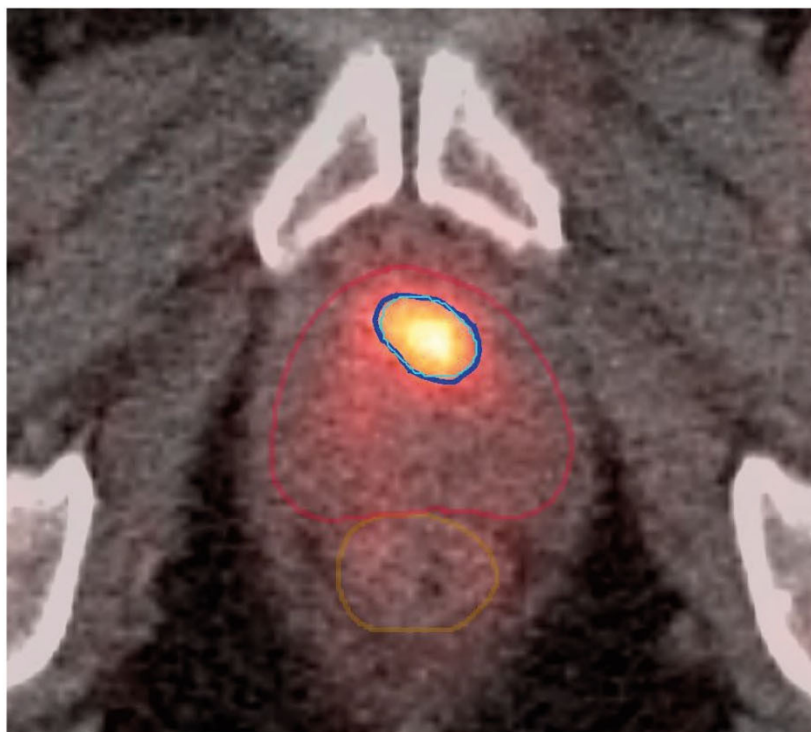
> 2014

D

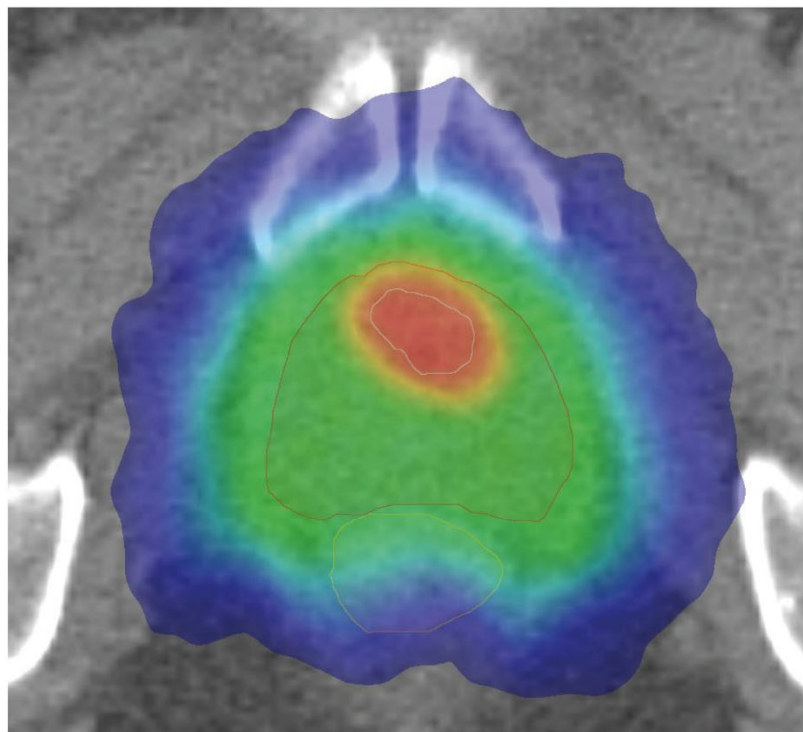
B

IMRT/VMAT dans les tumeurs prostatiques (PET-PSMA)

a)

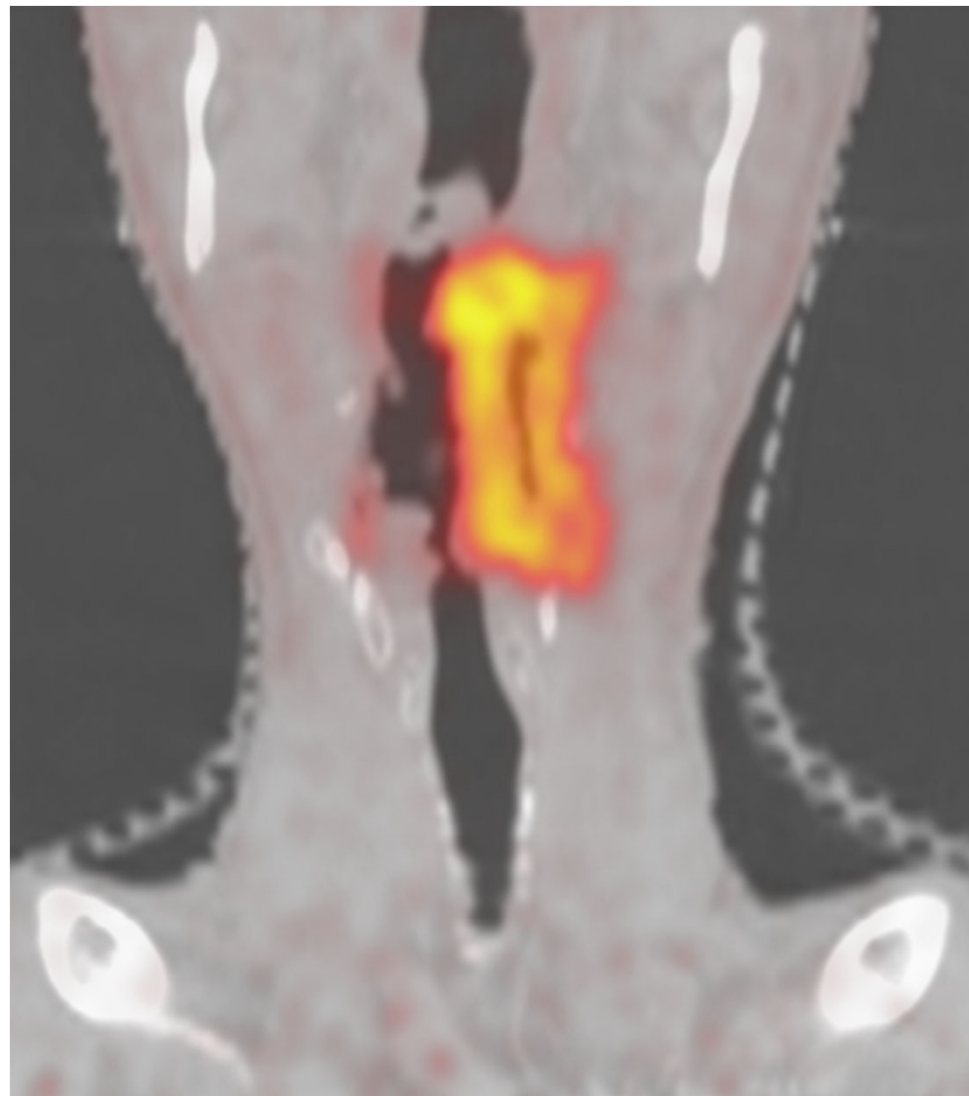
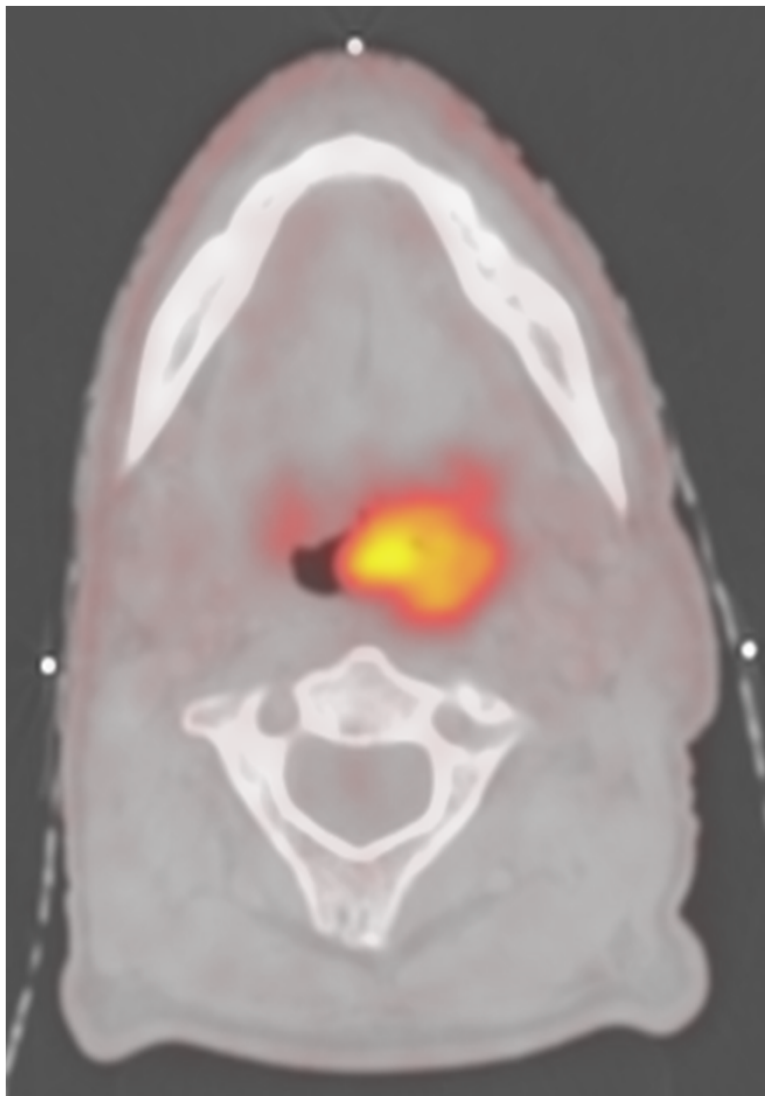


b)



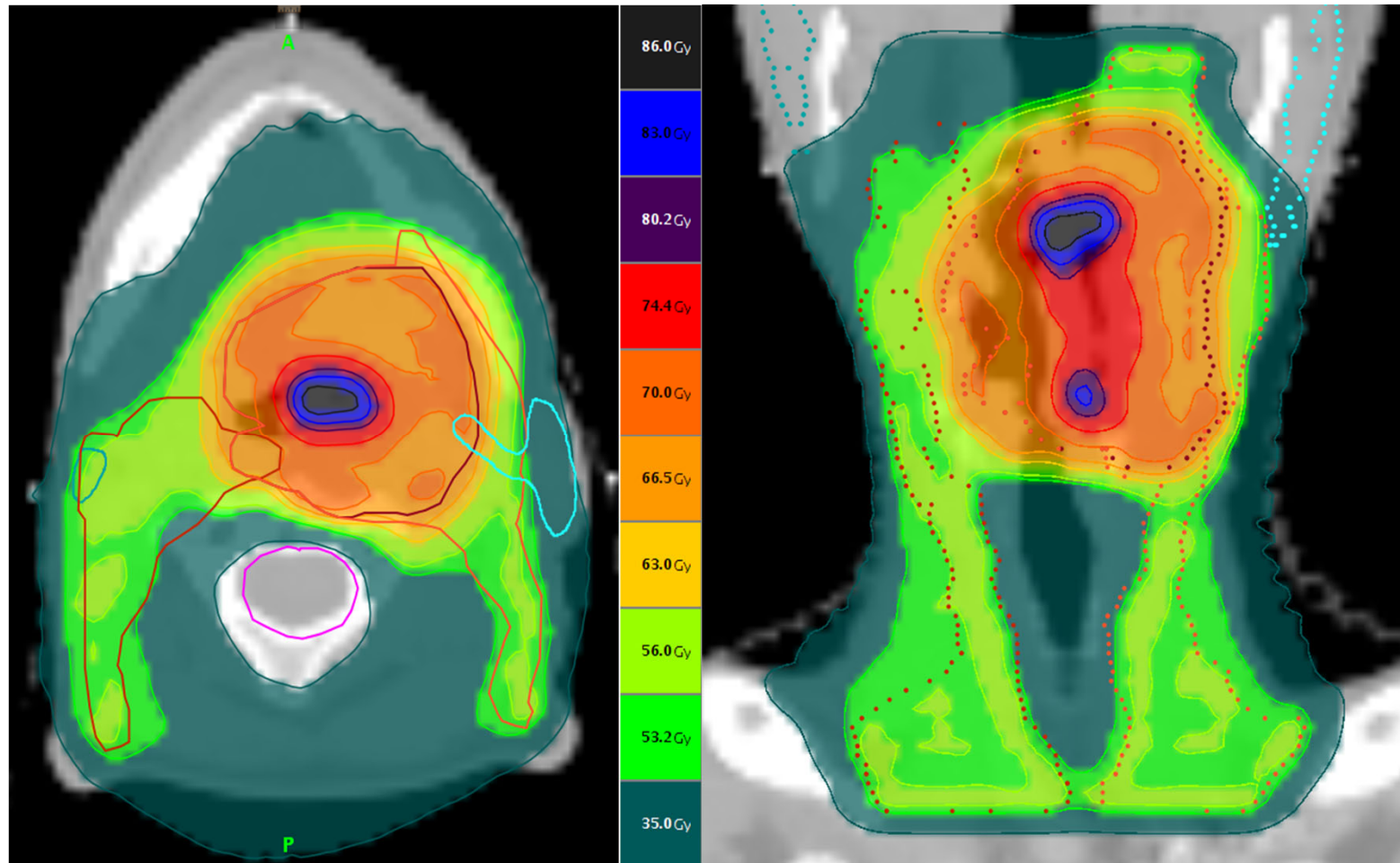
B

Hétérogénéité tumorale (FDG-PET)



B

Dose-painting



Oropharynx: T4b-N0-M0 – FDG-PET-CT

B

La protonthérapie...?

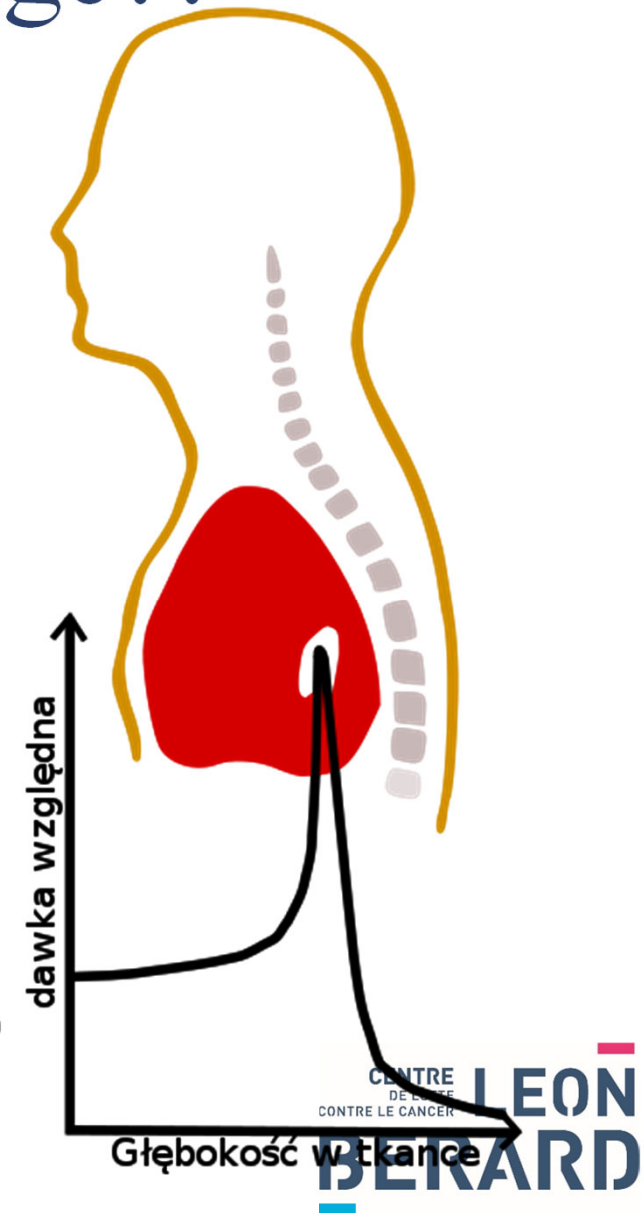
I



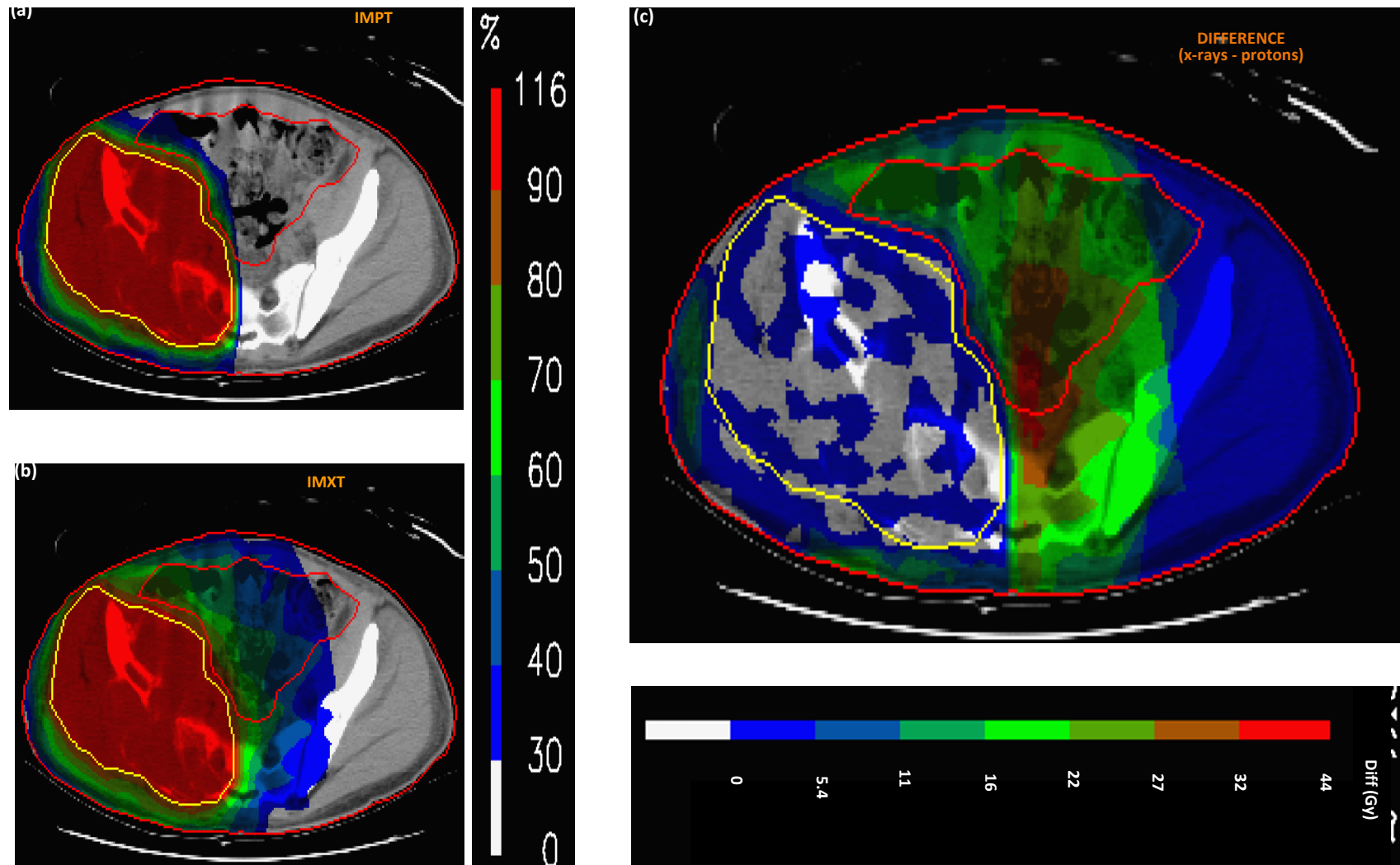
A

Quel est l'avantage??

- La masse des protons est bien plus grande que celle des électrons
 - Moins de diffusion latérale (donc moins de dispersion)
- Le trajet est limité par l'énergie
 - Et donc la dose est localisée à la profondeur voulue.
- La dose est très élevée en fin de trajet (pic de Bragg).



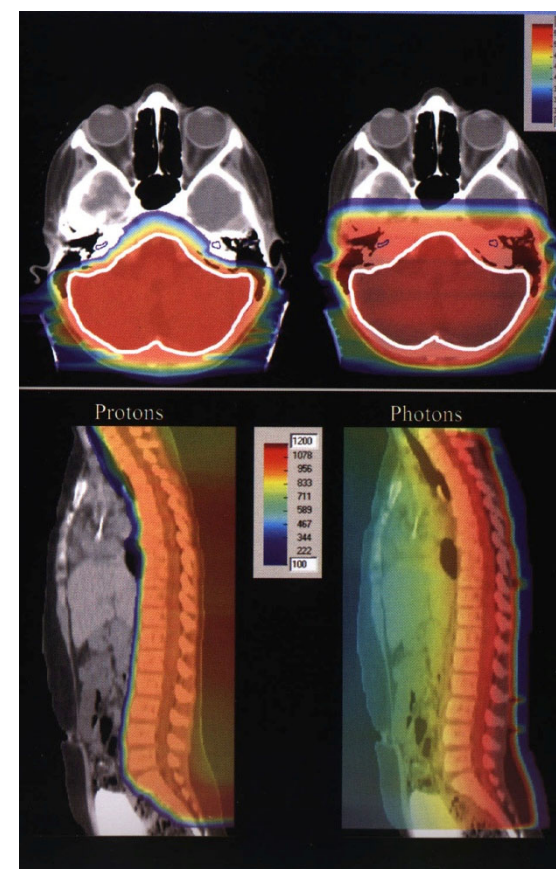
B IMRT et IMPT pour un sarcome d'Ewing



B

Indication principale: pédiatrie

	2000	2001	2003
leukemia	85	108	90
lymphoma	39	43	34
Embryonal tumours	52	54	63
CNS	94	68	65
Bone	15	18	24
STS	35	34	35
total	320	325	313



Medulloblastome chez un
enfant de 5 ans
4 MV photons vs. protons

Recrutement potentiel en France de ± 600 cas/ selon les
pratiques actuelles

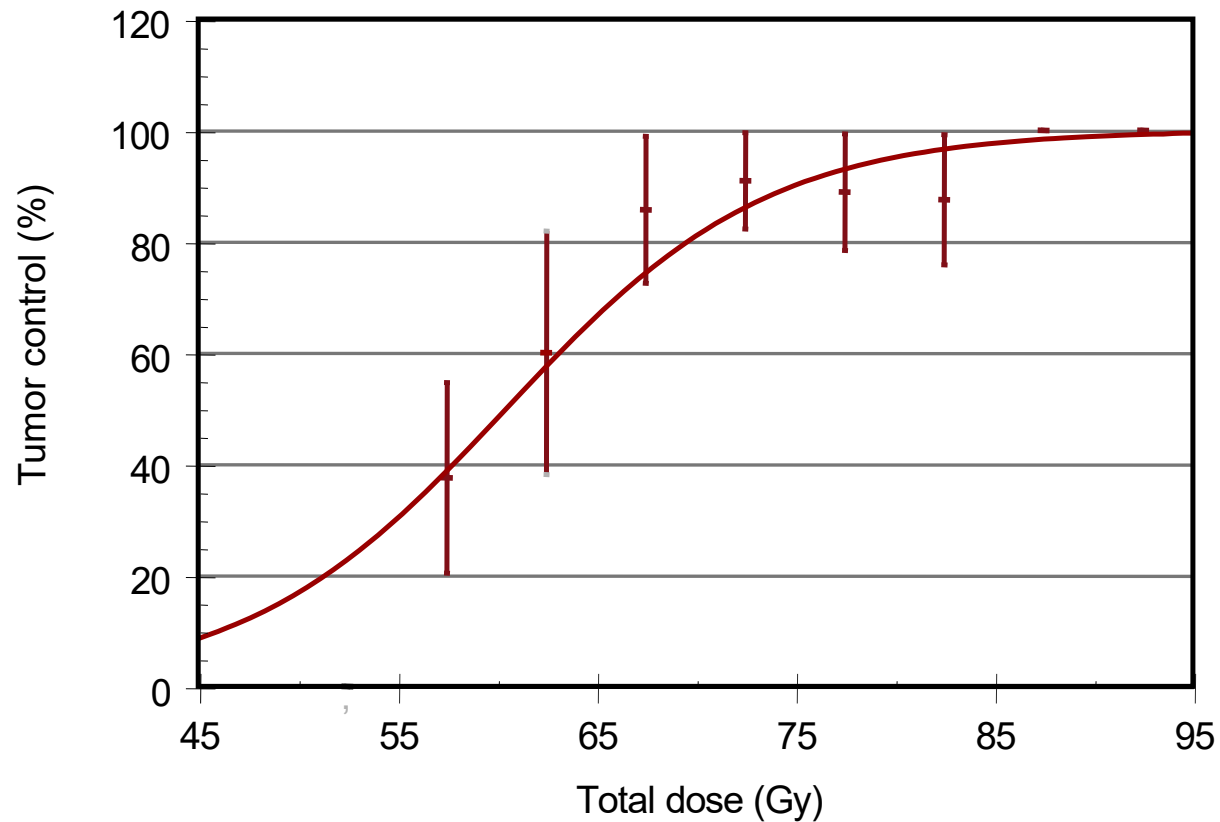


Clinical considerations: efficacy and toxicity of radiotherapy

A

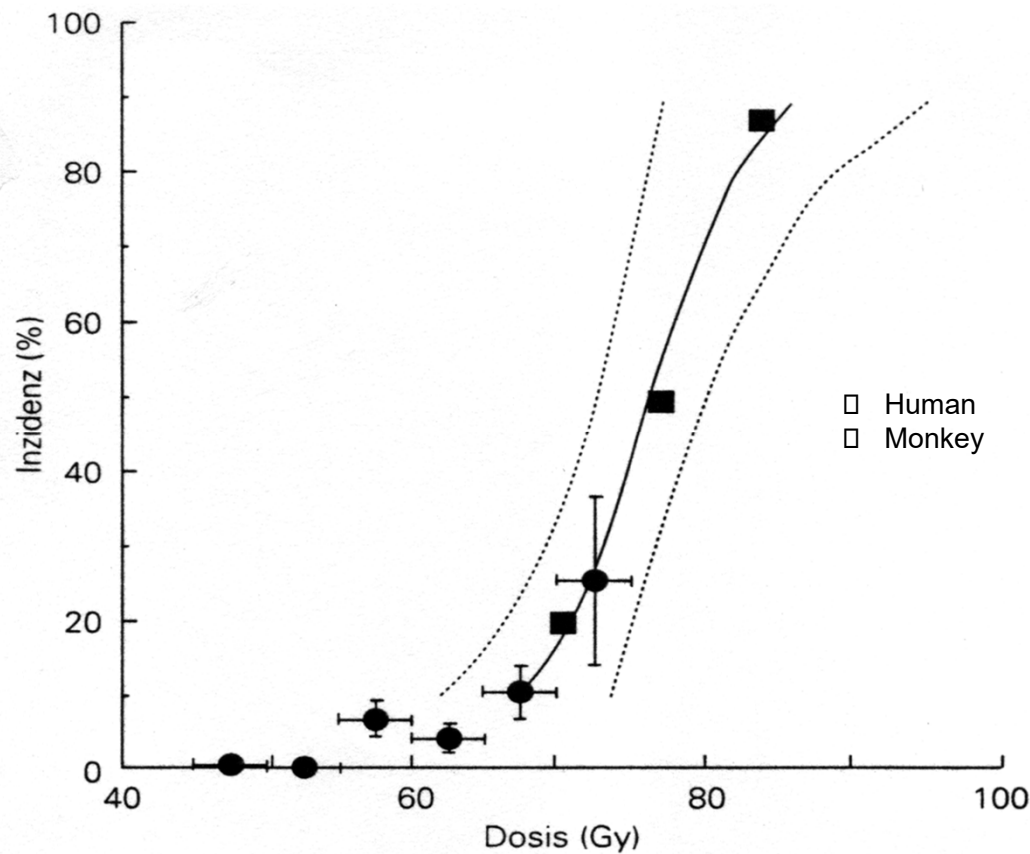
Tumor Control Probability (TCP)

Dose-response curve for neck nodes ≤ 3 cm



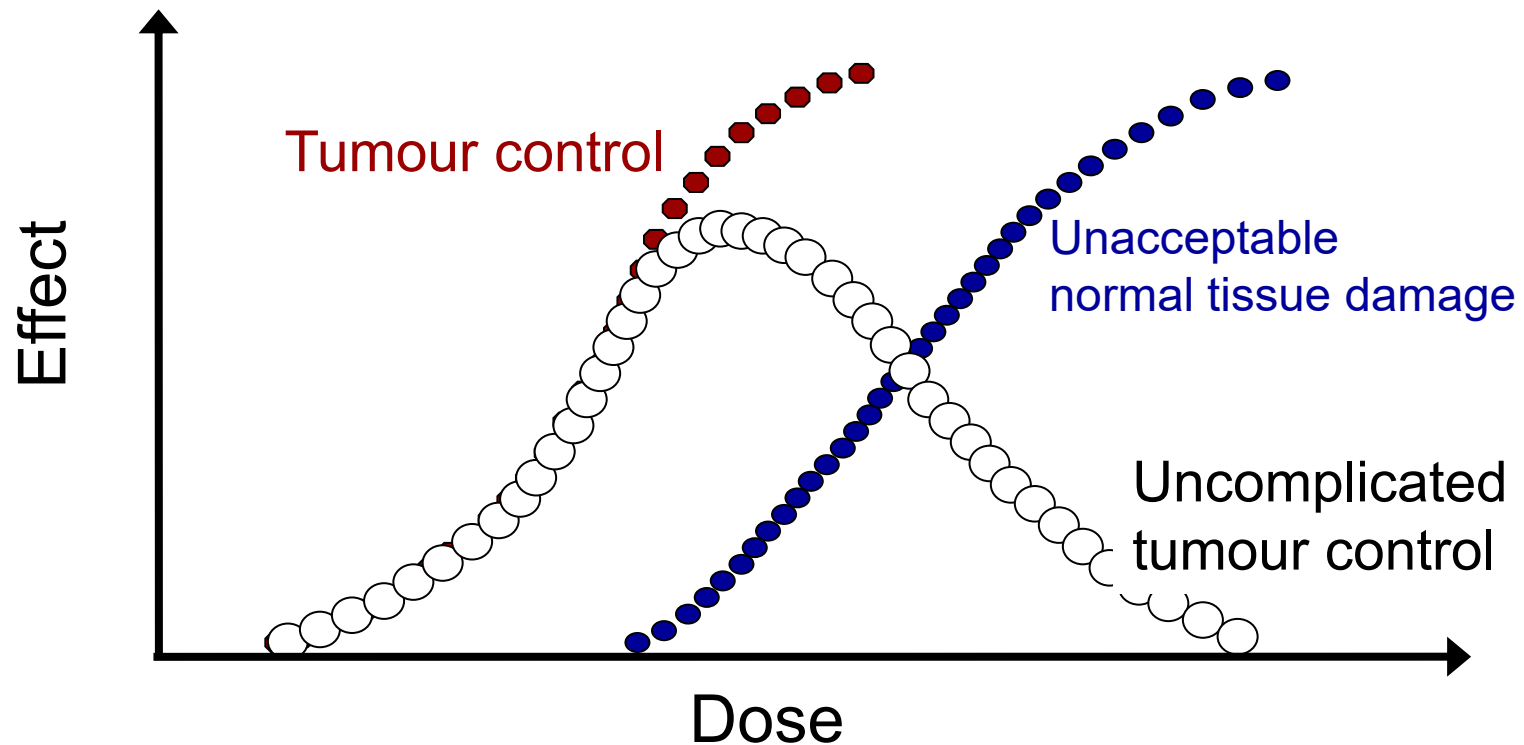
A

Normal Tissue Control Probability (NTCP)



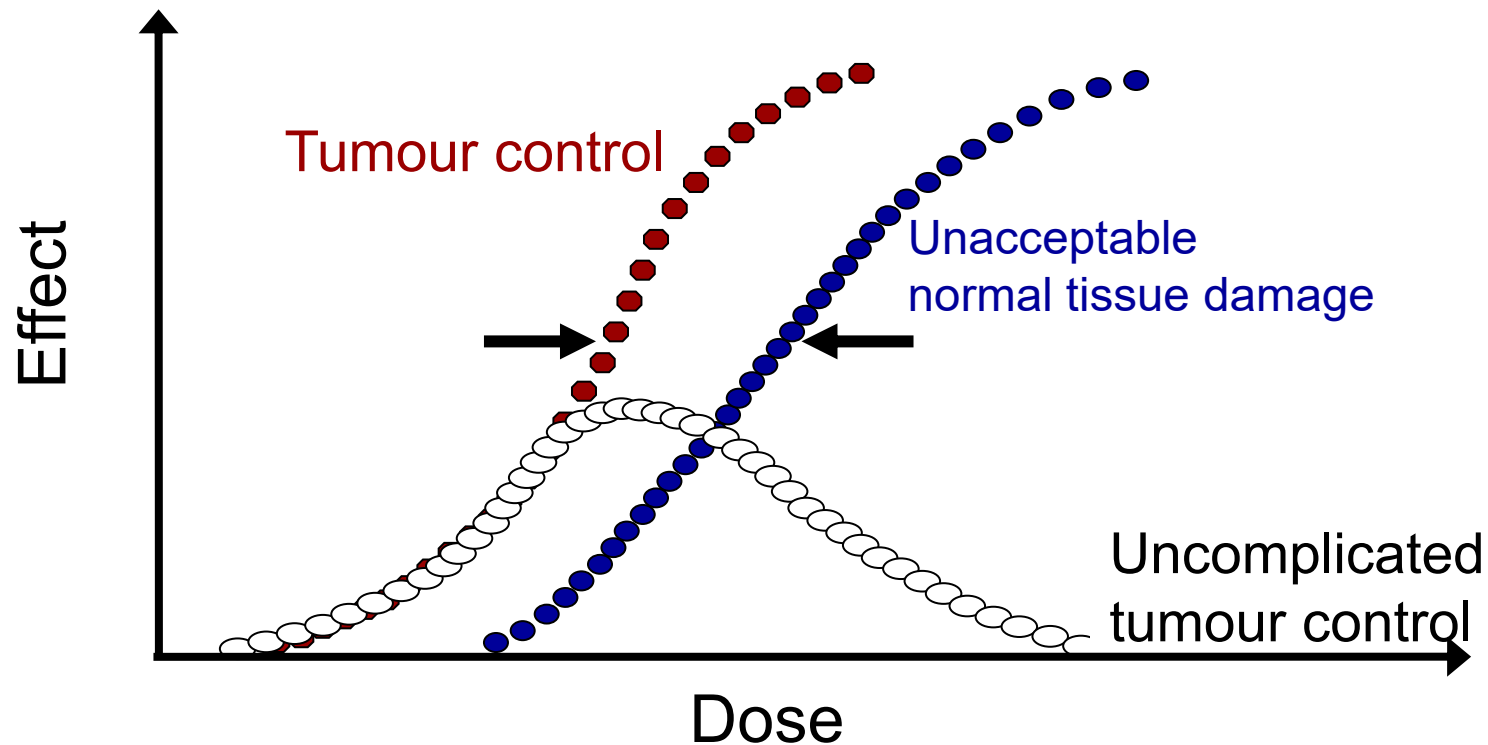
A

Uncomplicated tumor control: Therapeutic Ratio



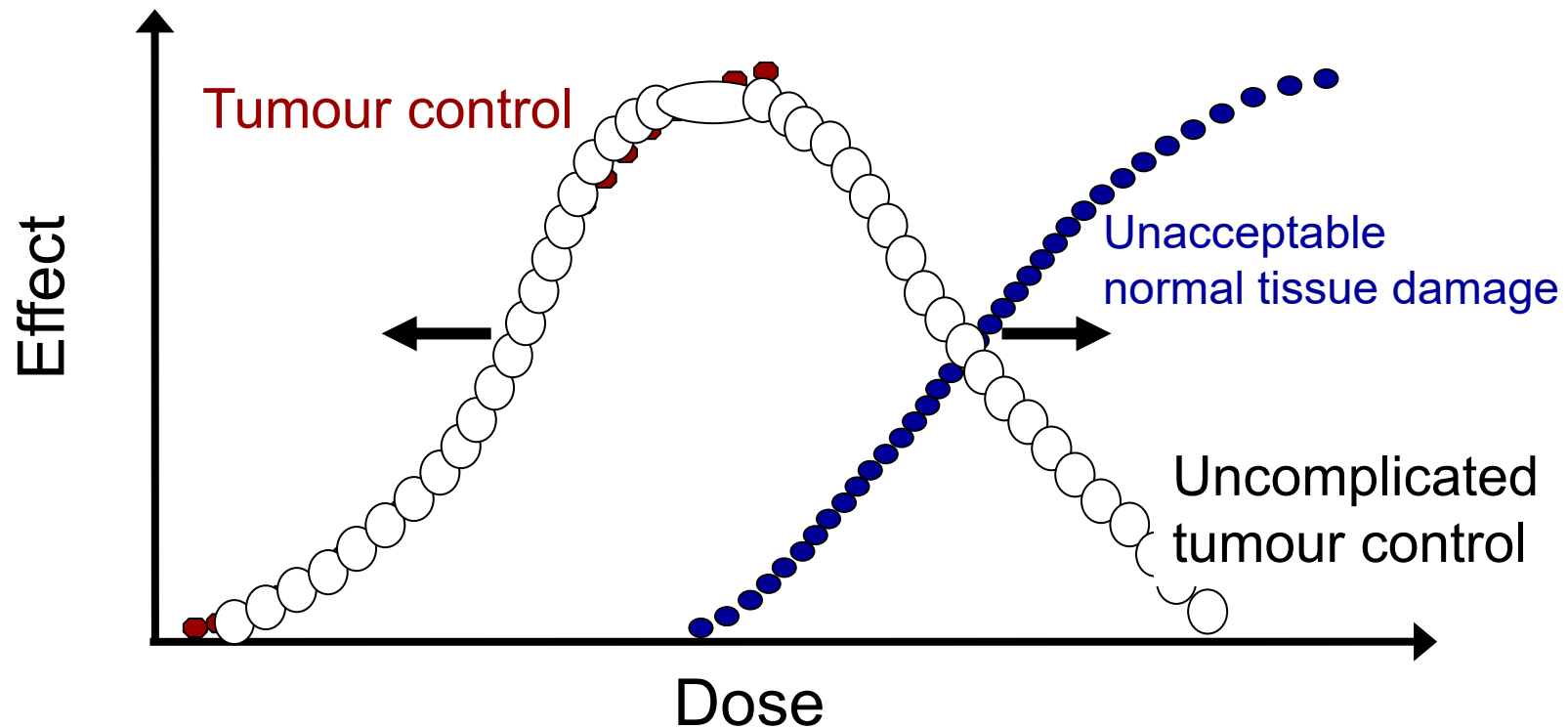
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Uncomplicated tumor control: Therapeutic Ratio

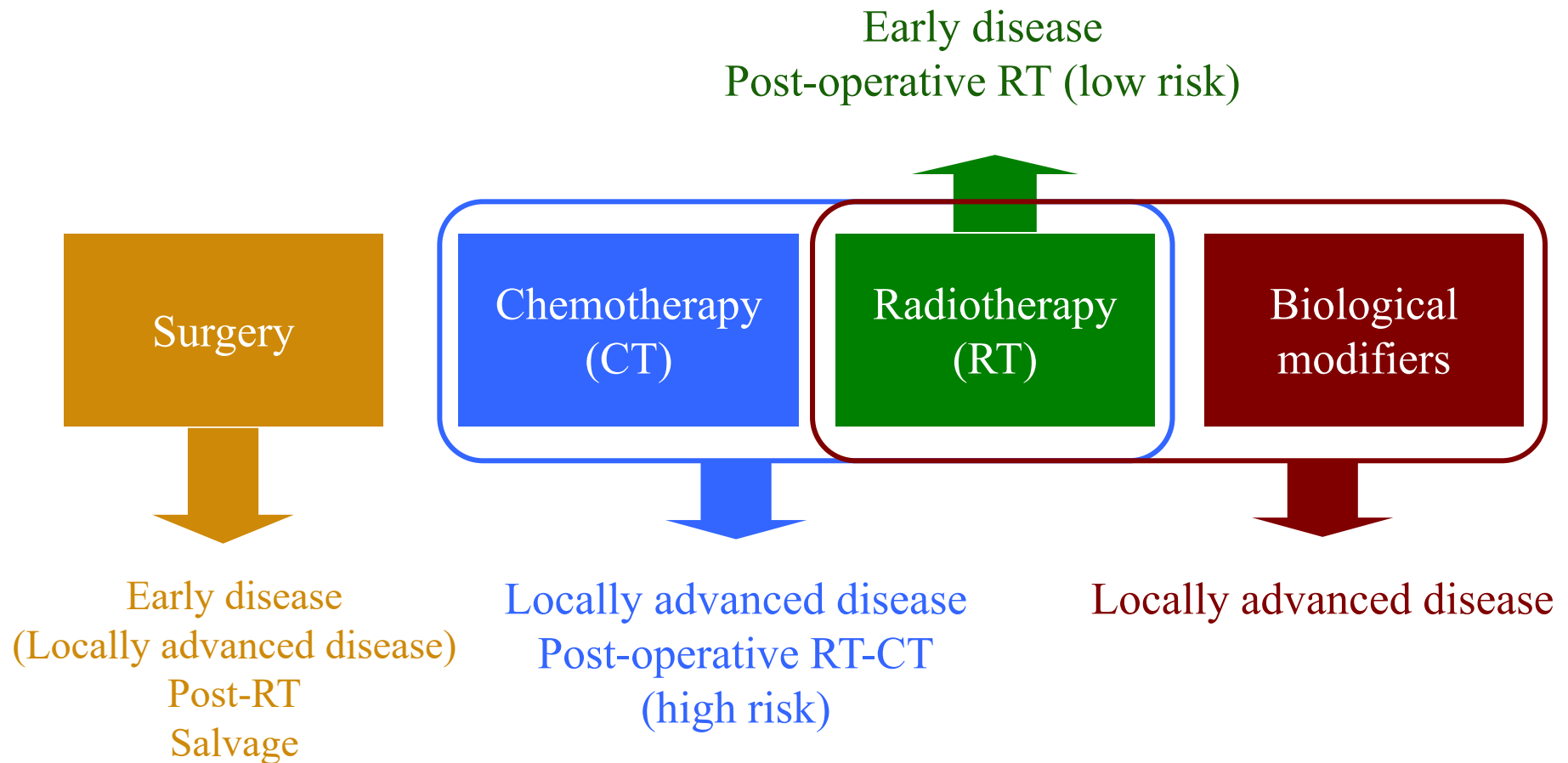


B

Uncomplicated tumor control: Therapeutic Ratio



A Radiotherapy in the armamentarium of cancer treatment



Conventional fractionation

1.8 – 2.0 Gy per fraction, 5 fractions per week

||||| ||||| ||||| ||||| ||||| ||||| |||||

	Example	Dose (Gy)	Tumor control (%)
<i>Sensitive</i>	Seminoma, Lymphoma	≤ 45	≥ 90
<i>Intermediate</i>	SCC, Adeno-Ca	50	≥ 90 (subclinical)
		60	~ 85 ($\varnothing$ 1 cm)
		70	~ 70 ($\varnothing$ 3 cm)
<i>Resistant</i>	Glioblastoma	≥ 60	~ 30 ($\varnothing$ 5 cm) none?
	Melanoma	≥ 60	none?

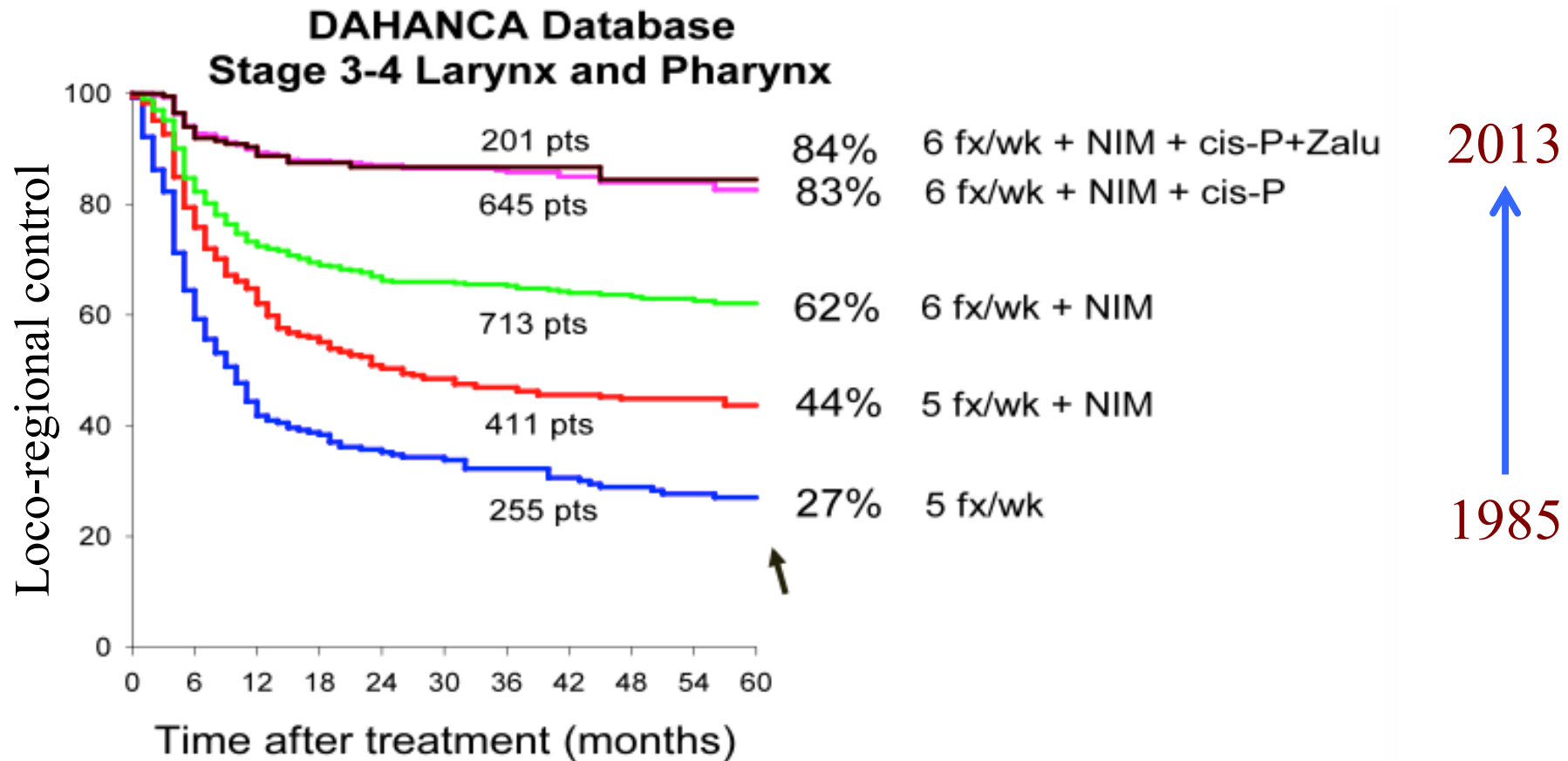
Indications

Traitements curatifs loco-régionaux de première intention $\pm$ chimiothérapie / biological modifiers

- T cérébrales, ORL, oesophagiennes, pulmonaires, prostatiques, hématologiques, digestives, cutanées, testiculaires, gynécologiques, ...
- Patients non-opérables, e.g. patient âgé, avec co-morbidité, ...
- Tumeurs non-résécables (e.g. localement avancées)
- “organ preservation strategy” (par ex. T du larynx, T de la marge anale)

B

The DAHANCA strategy: progression through consecutive clinical trials



DAHANCA.dk



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Overgaard et al., 2016

Indications

Traitements curatifs loco-régionaux adjuvants $\pm$
chimiothérapie / biological modifiers

- T cérébrales, ORL, oesophagiennes, pulmonaires, mammaires, prostatiques, hématologiques, digestives, cutanées, testiculaires, gynécologiques, sarcomes, ...

Indications

Traitements curatifs loco-régionaux neo-adjuvants
± chimiothérapie / biological modifiers

- T du rectum, gynécologiques, sarcomes, ...

Indications

Traitements palliatifs

- Objectifs: retarder l'évolution fatale et/ou soulager un symptôme
- Exemples: - métastases osseuses douloureuse: e.g. 1 x 8 Gy
 - métastases osseuses unique: RxTh stéréotaxique, e.g. 3 x 10 Gy
 - métastases pulmonaire unique: RxTh stéréotaxique, e.g. 3 x 10 Gy
 - saignement vésical: 1 x 8 Gy
 - métastases cérébrales: irradiation pan-craniène ou stéréotaxique

Prototypes of modified fractionation regimens

- Normo-fractionation

|||| | ||| | ||| | ||| | ||| | ||| | ||| | 70Gy/ 2.0 Gy/ 7w

- Hyperfractionation (e.g. H&N)

|||| | ||| | ||| | ||| | ||| | ||| | ||| | ||| | ||| | ||| | 80.5Gy/ 2x1.15 Gy/ ti=6h/ 7w

- Accelerated fractionation (e.g. H&N)

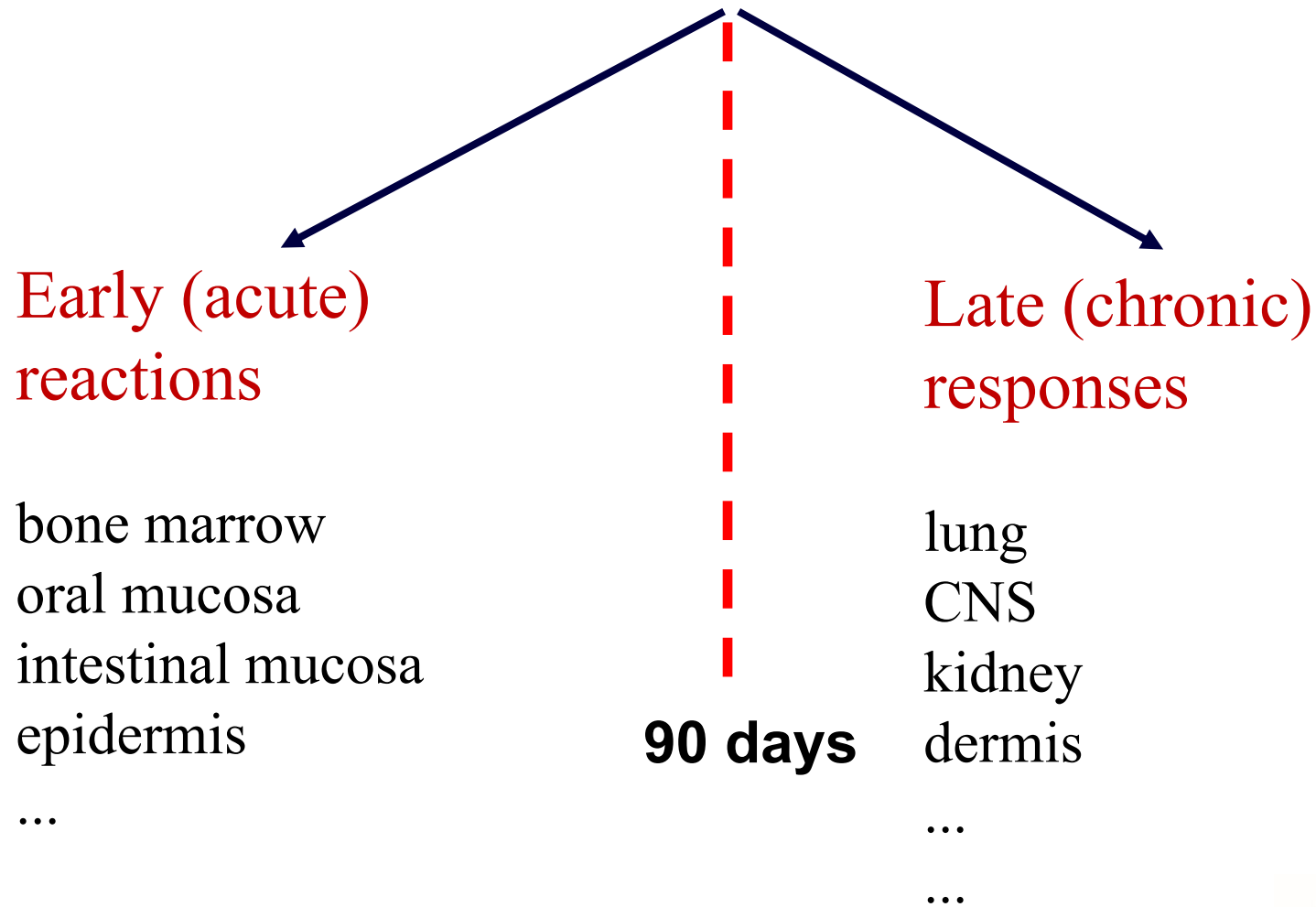
|||| | ||| | ||| | ||| | ||| | ||| | ||| | 70Gy/ 2.0 Gy/ 5w

- Hypofractionation (e.g. breast, prostate, paliation)

|||| | 67.5 Gy/13.5 Gy/ 2w |||| | ||| | ||| | ||| | ||| | 75Gy/ 2.5 Gy/ 5w

B

Radiotherapy side effects



A

Toxicité aiguë de la radiothérapie

- Cutanée

- Erythème (15-20 Gy)

- Epithélite exsudative

- R/ pommade calendula, éosine aqueuse

- Muqueuse

- ORL : mucite, xérostomie, oesophagite, agueusie

- R/ bains de bouche (alcalins +/- antifongiques), prophylaxie dentaire, antalgie, alimentation

- Digestive : ténesme, diarrhées, anite, poussée hémorroïdaire, rectite

- R/ locaux, anti-diarrhéiques

- Vésicale & uréthrale : cystite radique

A

Toxicité aiguë de la radiothérapie

- Hématologique : si volume important de moelle osseuse irradiée (e.g. bassin + rachis)
 - Anémie, lymphopénie, thrombopénie
R/ transfusion, ⚠⚠⚠ facteurs de croissance, ...
- Digestive
 - Vomissements, nausées
R/neuroleptiques, sétrons si besoin
- Pulmonaire : pneumopathie radique aigue
R/ corticoïdes
- Neurologique : HTIC si RTE cérébrale
R/ corticoïdes, mannitol, ...

A

Toxicité tardive de la RTE : fibrose

- Cutanées : pigmentation modifiée, fibrose, (alopécie rarement définitive)
- Cardiaque : insuffisance cardiaque, péricardite, ischémie coronarienne
- Digestives : sténose post-radique (œsophage), grêle radique, recto-colite radique
- Urologique : vessie radique, sténose urétérale (rare)
- ORL : xérostomie, ostéoradionécrose, séquelles trophiques

Toxicité tardive de la RTE

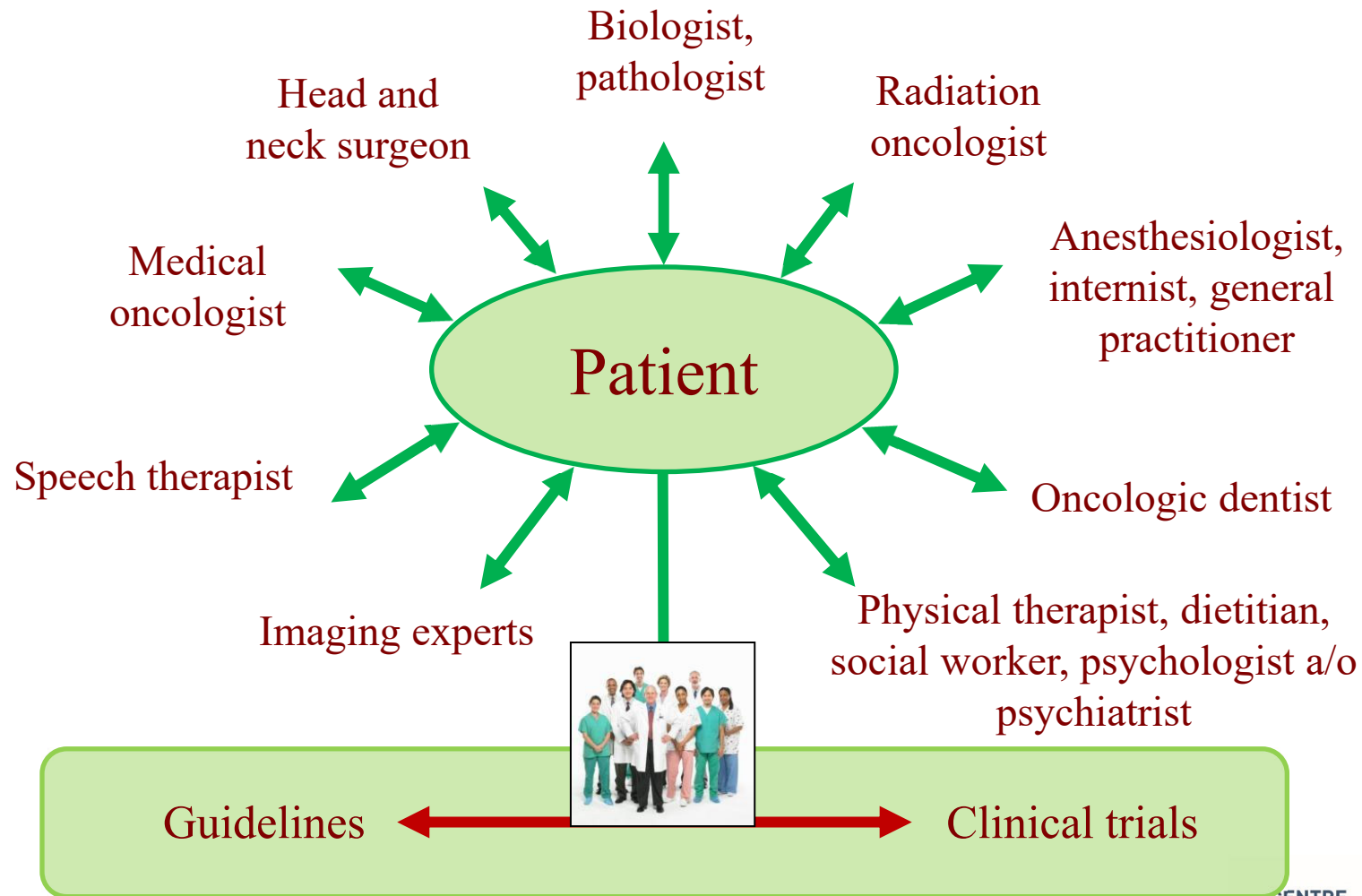
- Neurologique
 - cérébrales : encéphalopathie radique, radionécrose cérébrale
 - myelopathie radique : obsession +++
 - plexite radique
- Troubles de croissance
- Troubles endocriniens
 - Hypophyse : panhypopithuitarisme
 - Thyroïde : hypothyroïdie
 - Gonades : stérilités
- Cancers radio-induits (<1%)
 - Sarcomes ++
 - 3-30 ans
 - En champ irradié

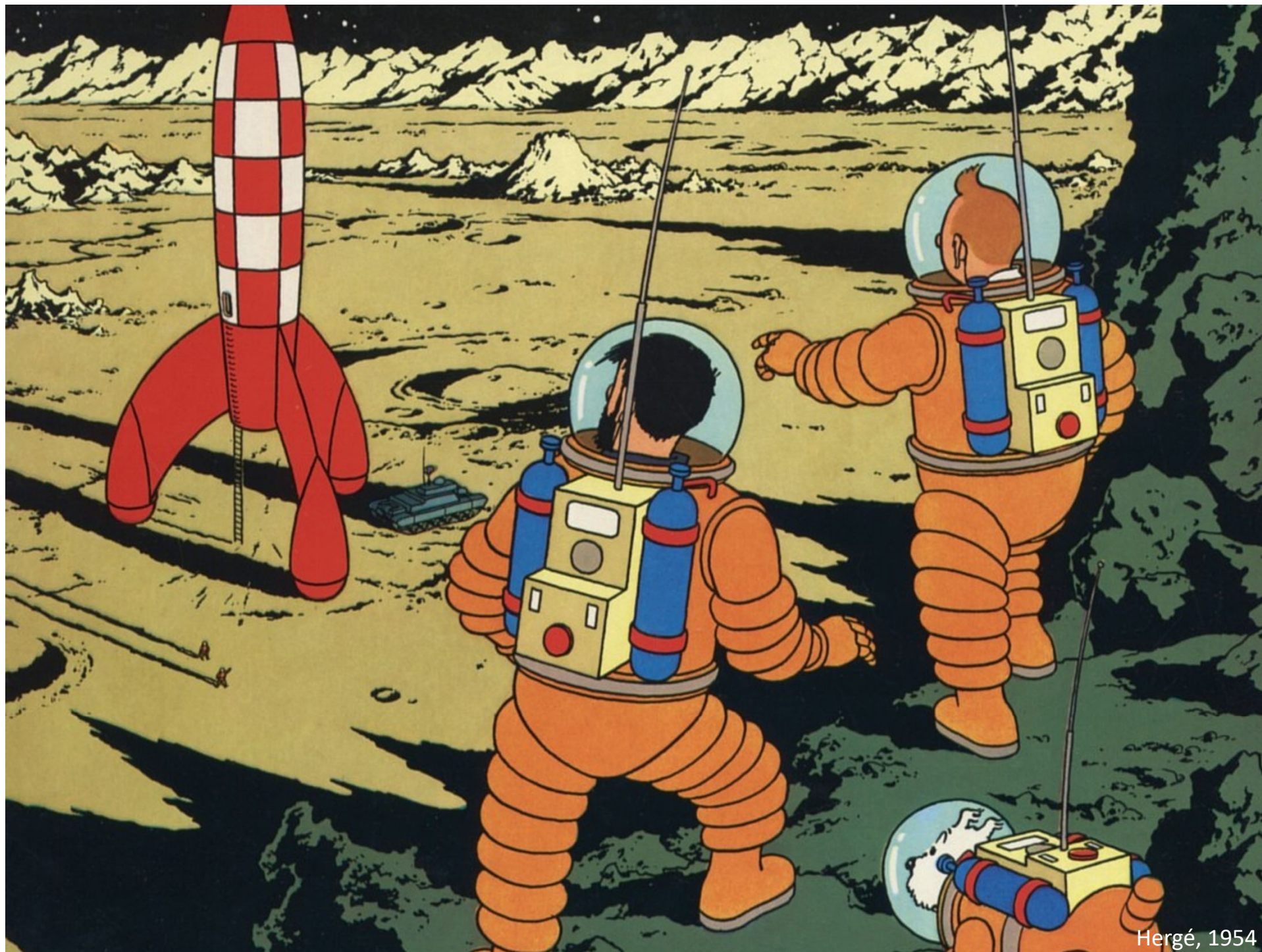


Conclusions

A

Multidisciplinary patient management





Hergé, 1954