Ultrahypofractionation : Hope or Hype

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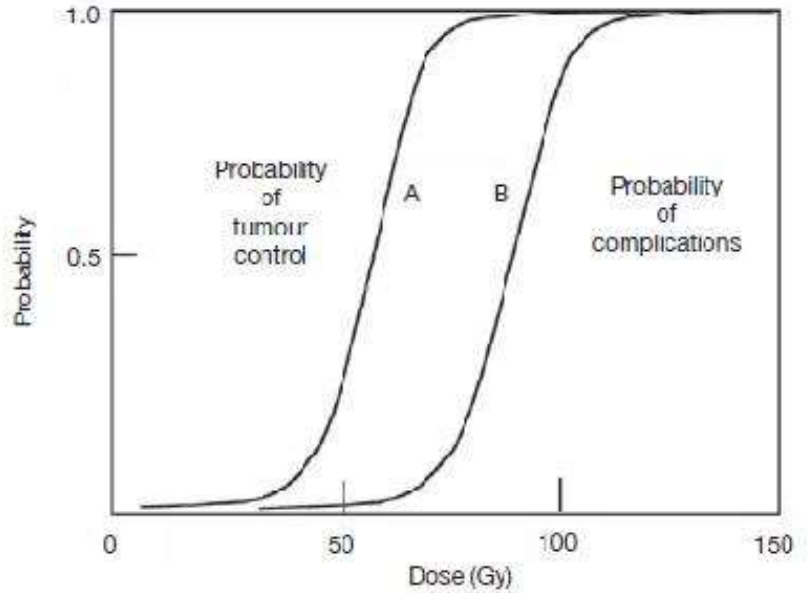


FIG. 14.4. The principle of therapeutic ratio. Curve A represents the TCP, curve B the probability of complications. The total clinical dose is usually delivered in 2 Gy fractions.

The Four "R" of Radiotherapy

- Reoxygenation
- Repopulation
- Reassortment
- Repair

The 4 Rs form the basis of fractionated radiotherapy.

Fractionation spares normal tissues because of repair of SLD b/w dose fractions & repopulation of cells.

Fractionation increases damage to the tumor because of reoxygenation & reassortment of cells into radiosensitive phases of cycle b/w fractions.

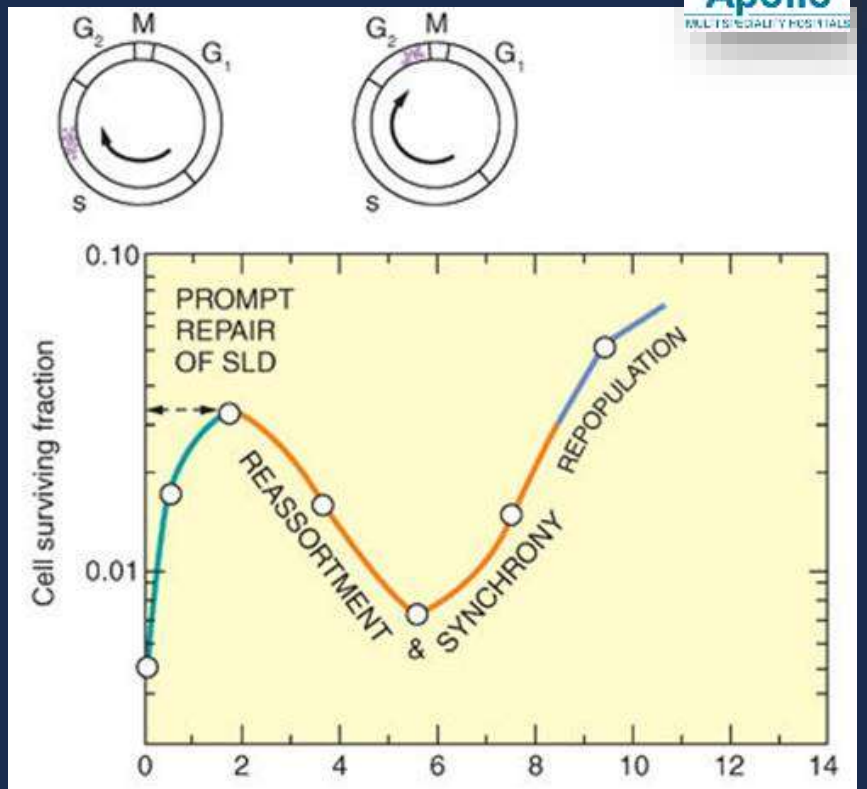
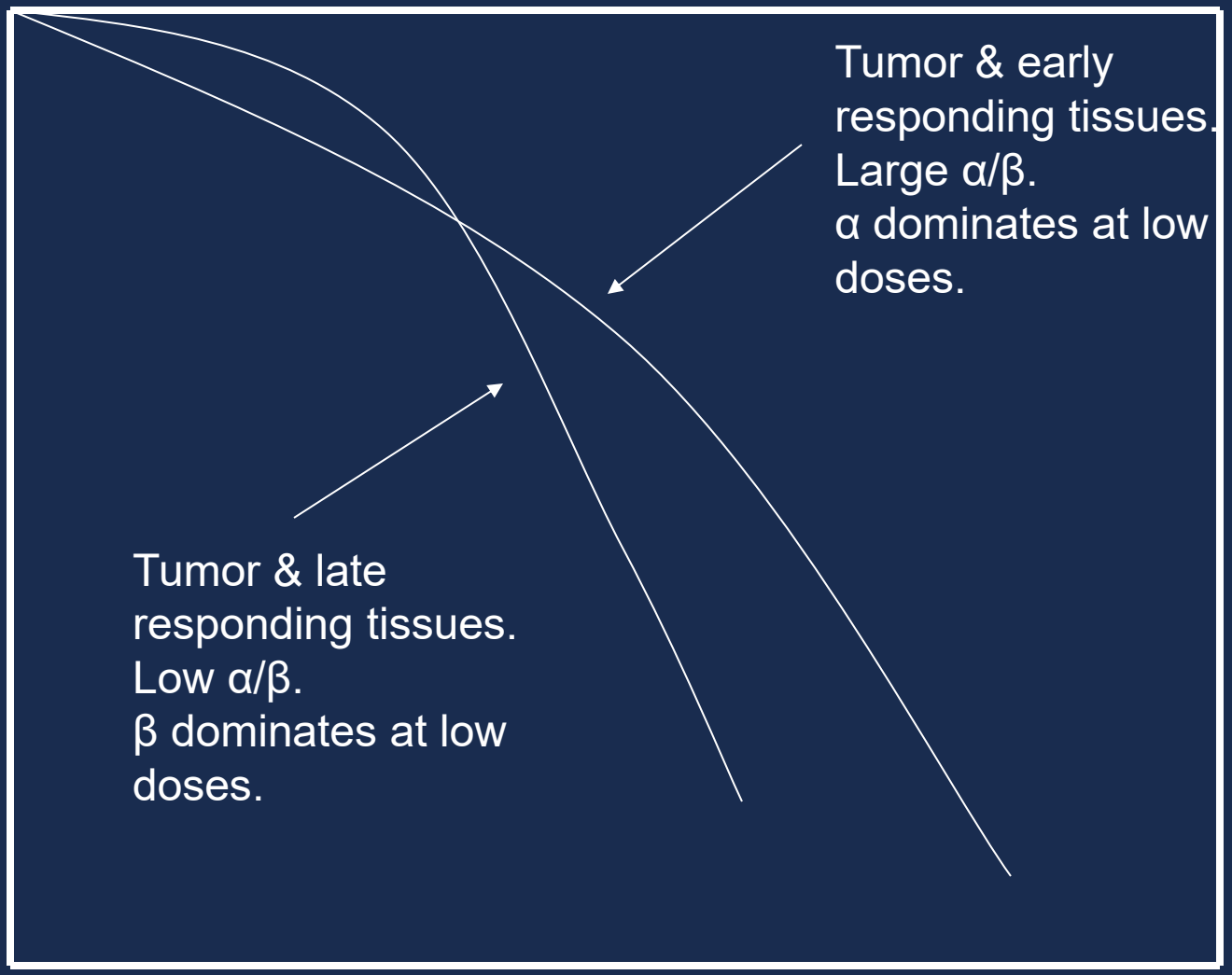
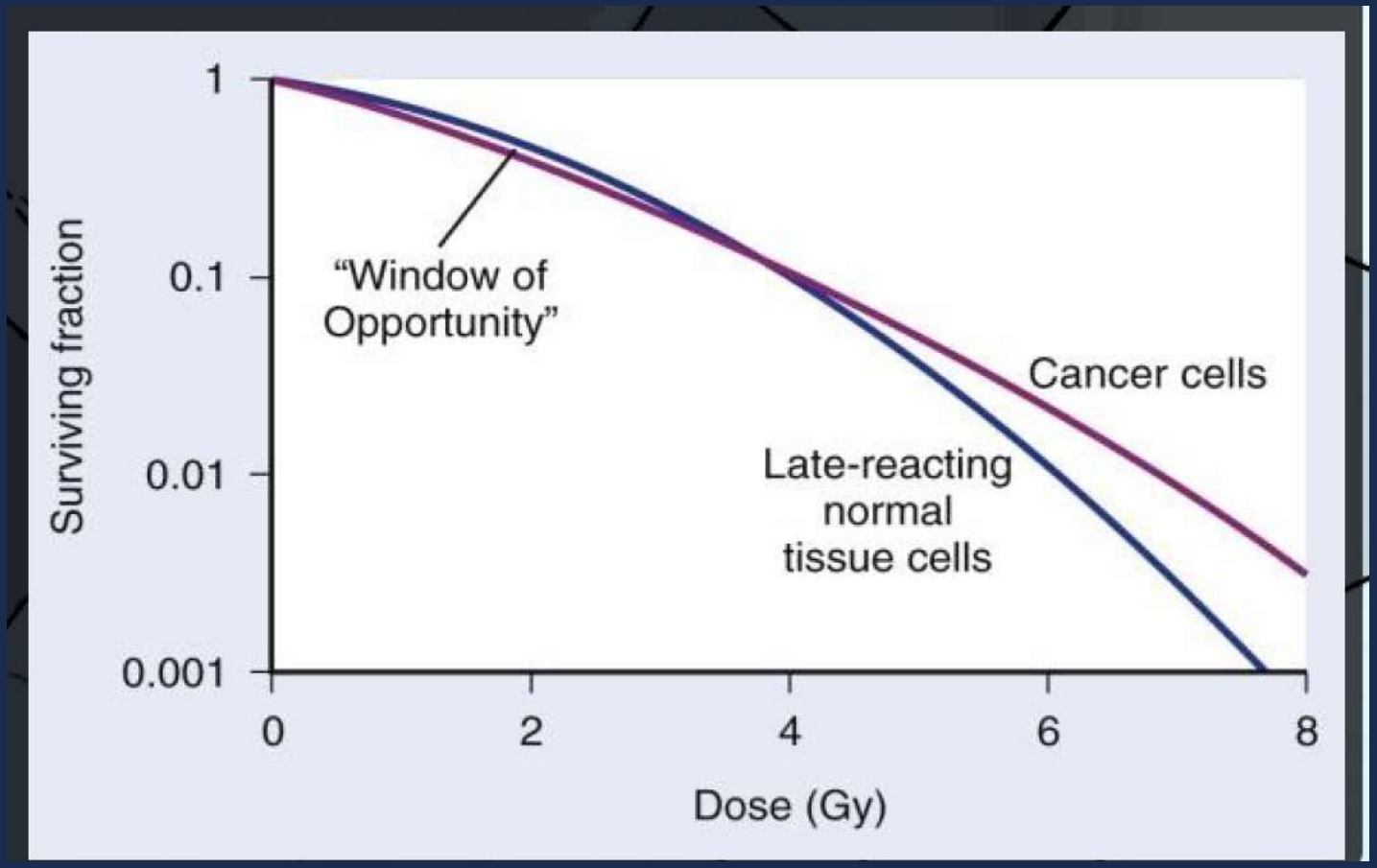
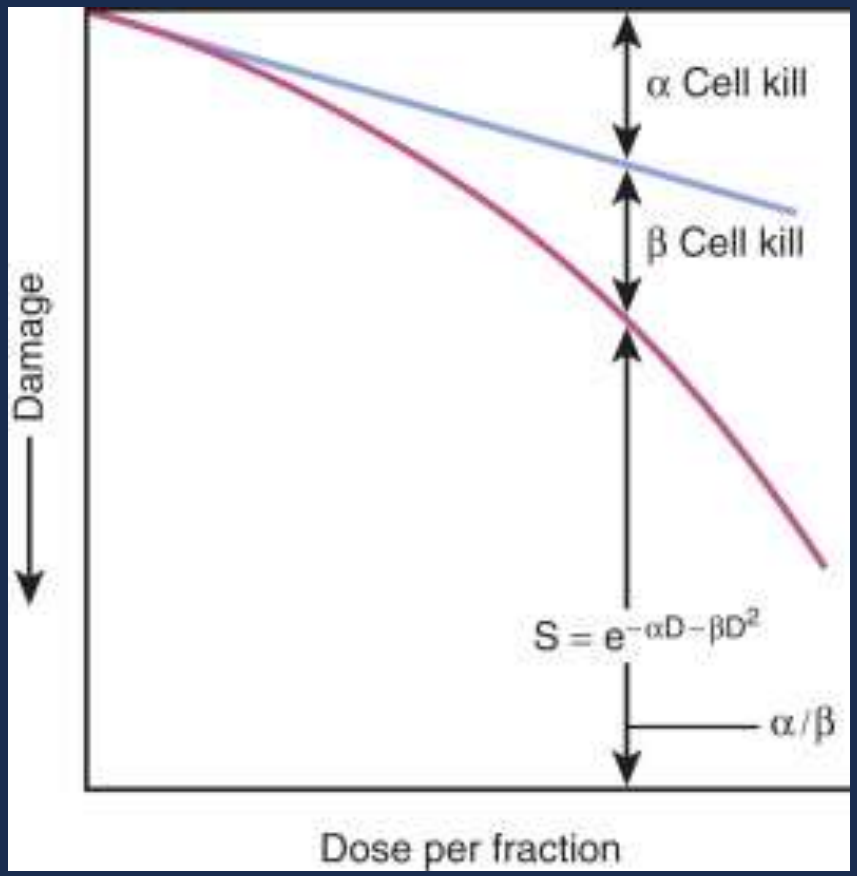


Figure 13.11 Idealized survival curve of rodent cells exposed to two fractions of x-rays. This figure illustrates how the time interval between doses alters the sensitivity of cells when exposed to multiple fractions. In this case, cells move from a resistant phase of the cell cycle (late S phase) to a sensitive phase of the cell cycle (G2 phase). This is known as *reassortment*. If longer periods of time occur between fractions of radiation, cells will undergo division. This latter process is called *repopulation*. SLD, sublethal damage. (From Hall EJ, Giaccia AJ. *Radiobiology for the Radiologist*. Philadelphia: Lippincott Williams & Williams; 2012, with permission.)

Dose Response Relationship




1
0.1
0.01
0.001
Surviving fraction
"Window of Opportunity"
Cancer cells
Late-reacting normal tissue cells
0
2
4
6
8
Dose (Gy)



α/β for Head and neck cancer =10 Gy

α is the component of cell killing proportional to the dose.

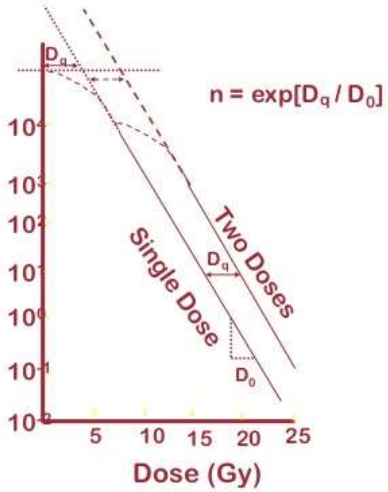
β is the component of cell killing proportional to the square of the dose.
D = the dose at which α = β

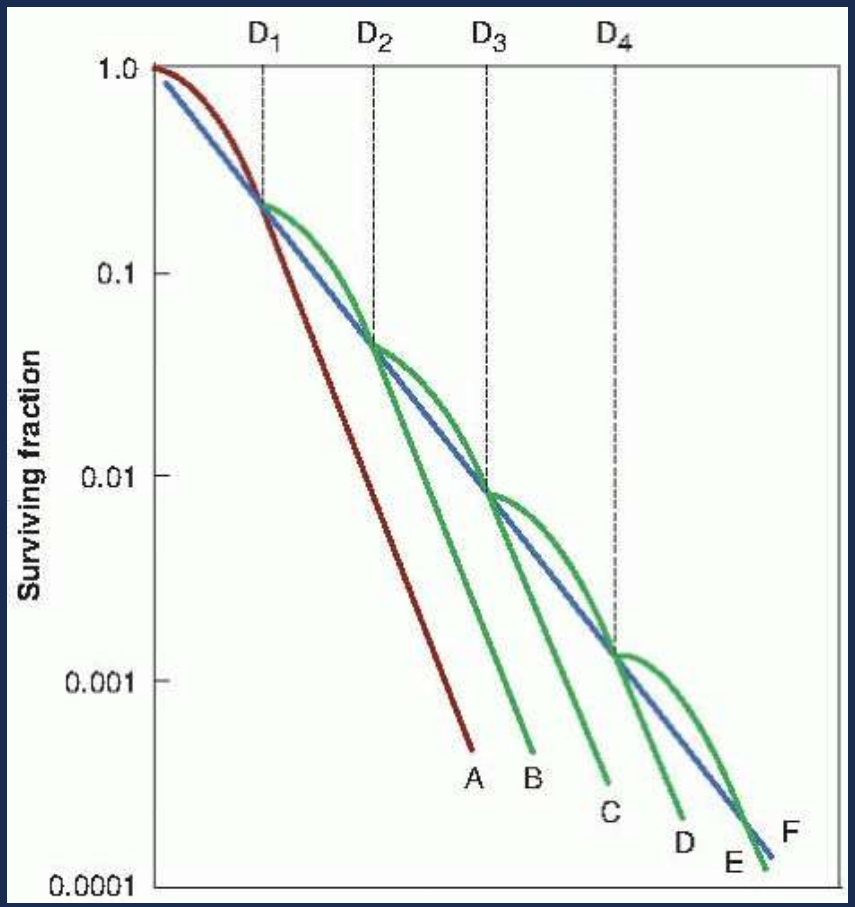
Therefore α/β is the dose at which, the linear and quadratic component of cell killing are equal.

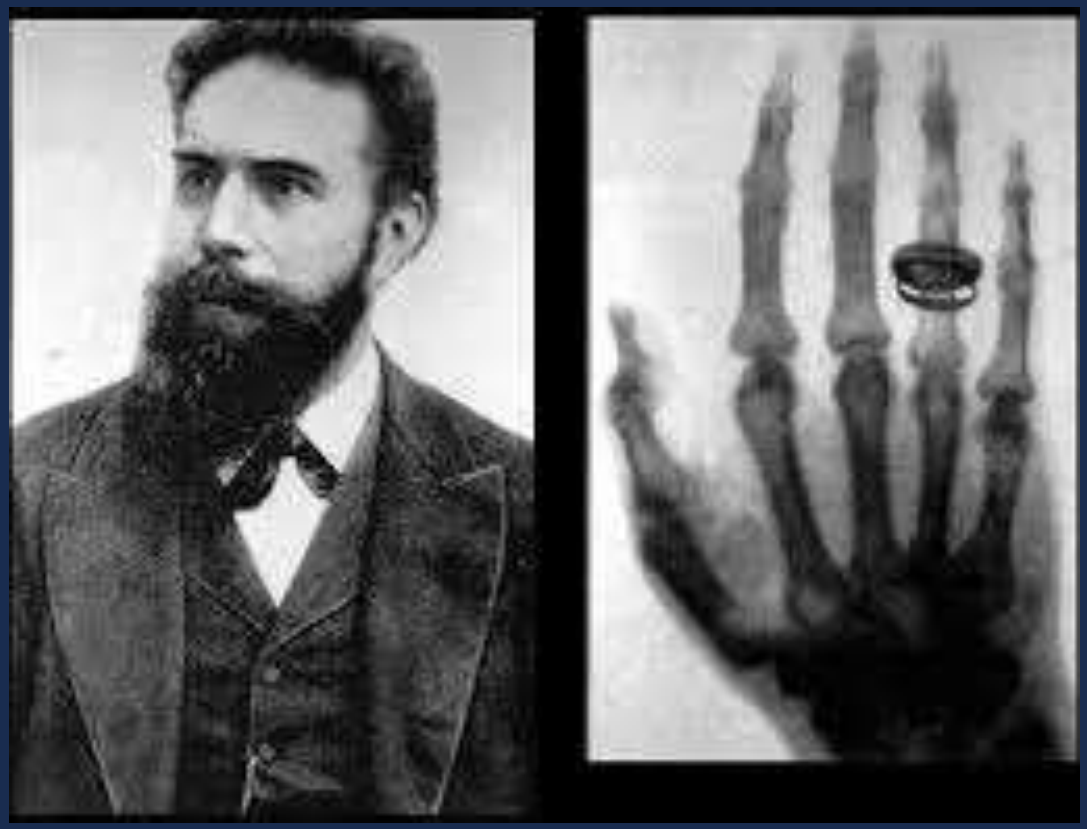

सौ सोनार की,
एक लोहार की
A goldsmith's
hundred,
blacksmith's
one.
www.QuoteWorld.in

Fractionation

- If the dose is delivered as equal fractions with sufficient time ,repair of sub-lethal damage ocurs
- Elkind' s Recovery takes place between radiation exposure , cell act as fresh target.
- Elkind & Sutton showed that when two exposure were given few hours apart ,the shoulder reappeared.







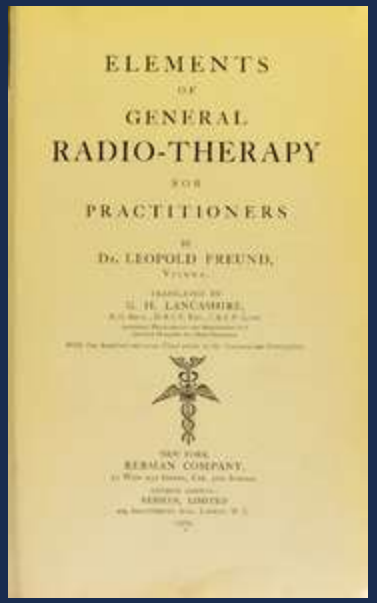
History

The first report on the new rays was heralded by W.C. Rontgen in November 1895 and his first written report was published at the end of December 1985. Within a few days the publicity in the German press reached London on January 6, 1896 and from there was cabled to newspapers all over the world

History

Just three weeks later, on January 29, 1896, E.H. Grubbe a vacuum tube manufacturer in Chicago used the new rays therapeutically for the first time, at the suggestion of Dr. Ludlam. The patient had breast cancer and was exposed to single treatment for about 1 h

History


ELEMENTS
OF
GENERAL
RADIO-THERAPY
FOR
PRACTITIONERS
BY
Dr. LEOPOLD FREUND,
VIENNA.

In Austria, the dermatologist Leopold Freund had among others observed epilation after exposure to x-rays. In 1896 he treated a patient with hairy nevus (3) daily over 2 weeks and was the first to give fractionated radiotherapy.

In 1914 the Austrian radiologist Gottwald Schwarz suggested that multiple doses would be more effective because the time of greater radiosensitivity was the time of mitosis

In 1918 Kroening and Friedrich showed that the dose necessary to produce the same skin reaction had to be increased when multiple fractions were used rather than just one

History

Early Fractionation

The first successful treatments for cancer were made with fractionated radiotherapy; not deliberately intentional, but due to the fact that the early x-ray tubes were low output devices and treatment needed to be repeated daily. Due to the lack of effective dosimetry for decades after the discovery of radiotherapy, skin reaction was the only way of determining the dose.

As the machines improved, Single fraction RT became possible in 1914 after the invention of coolidge cathode tube the ability to deliver higher doses over a shorter period of time became available and debate about the best way of delivering radiotherapy intensified.

The following ten years was a period of uncertainty about the proper way to fractionate.

Two schools of thought

- **ERLANGEN**
- **PARIS**

The Erlangen School

A group in Germany of which the most influential member was **Wintz** argued that single doses were the most effective, and that fractionated radiotherapy was "weak" and "primitive". Their rationale for single-fraction radiotherapy was based on their interpretation of the Bergonié–Tribondeau Law of radiation sensitivity, published in 1906,

which concluded: “From this law, it is easy to understand that roentgen radiation destroys tumors without destroying healthy tissues.” Therefore, it appeared that there was an inherent advantage of roentgen irradiation that might be lost if cancer cells were allowed time to recover.

Wintz and his colleagues argued that “recovery from radiation injury depends on cellular metabolism and a rapidly growing tumor cell is better able to affect recovery from injury than a connective tissue cell. Therefore, the difference in recovery will favor the tumor if the cancerocidal dose is not applied in the first treatment

This view of radiotherapy remained popular into the 1920s but increasing evidence of superior outcomes (higher cure rates and lower toxicity) gradually eradicated this method - at least until the introduction of stereotactic radiosurgery several decades later.

The Paris School

History

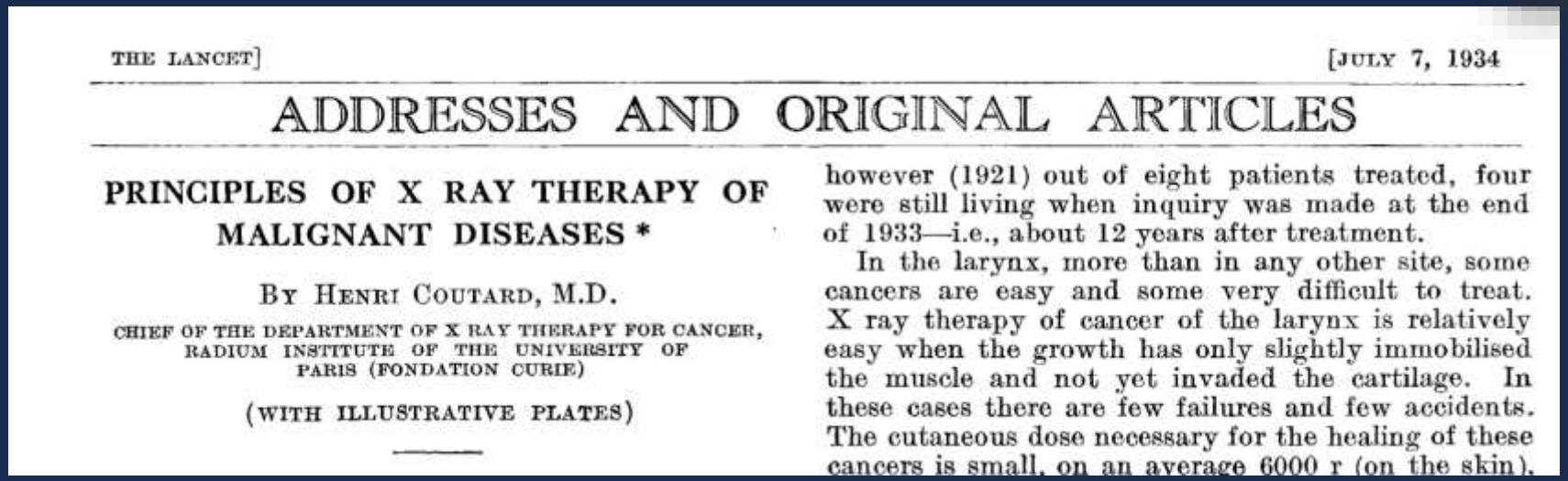
In 1930s, experiments were done by Regaud & colleagues in France. Rams could not be sterilized **with a single dose of X-rays, without extensive skin damage**.

If the radiation was delivered in daily fraction over a period of time, **sterilization was seen possible without skin damage.**

Testes was regarded as a model of growing tumor and skin as dose limiting normal tissue.

This led to the Coutard study that culminated in the fractionated EBRT techniques of today. (Lancet 1934; 2:1 – 8 Coutard H. Principles of X-ray therapy in malignant diseases.)

History



THE LANCET] [JULY 7, 1934

ADDRESSES AND ORIGINAL ARTICLES

PRINCIPLES OF X RAY THERAPY OF MALIGNANT DISEASES *

BY HENRI COUTARD, M.D.

CHIEF OF THE DEPARTMENT OF X RAY THERAPY FOR CANCER, RADIUM INSTITUTE OF THE UNIVERSITY OF PARIS (FONDATION CURIE)

(WITH ILLUSTRATIVE PLATES)

however (1921) out of eight patients treated, four were still living when inquiry was made at the end of 1933—i.e., about 12 years after treatment.

In the larynx, more than in any other site, some cancers are easy and some very difficult to treat. X ray therapy of cancer of the larynx is relatively easy when the growth has only slightly immobilised the muscle and not yet invaded the cartilage. In these cases there are few failures and few accidents. The cutaneous dose necessary for the healing of these cancers is small, on an average 6000 r (on the skin),

If the total dose, or the daily dose, or the intensity per minute has been too high, if the field has been too large in relation to the doses, or if the filtration or the tension has been too low, the connective tissue may be modified. The nutrition of the epithelioma cells thus becomes difficult. The cellular radiosensitivity, which seems to be linked up not only with the youthfulness of the cells but above all with the activity of their interchanges with the vasculoconnective tissue, is modified, often diminished, and sometimes suppressed. The cancer cells behave clinically as if they had become insensitive to the irradiations.

History

Alongside the energy factor, considered originally as the sole factor or at least essential to the X ray therapy of cancer, the daily repetition of irradiation in doses either uniform or unequal and the increase in the number of days of treatment, have provoked a second factor, the time factor.

Summary

The two principal factors in X ray therapy are the energy and the time. They must be considered in their relation to the cancer cells on the one hand, and on the other hand to the vasculo-connective tissue and the general tissues of the site from which the cancer is developing.

History

Beginning in 1919 Coutard treated incurable head and neck tumors with fractionated low dose roentgenotherapy. His methods were designed to mimic the low dosage radium technique of Regaud

At the International Congress of Otology in Paris in 1922 Regaud, Coutard and Hautant presented 6 patients with advanced carcinoma of the larynx treated by radiation therapy and now free of disease . This was the first time radiation therapy was shown to be an independent specialty practiced not by surgeons but by radiation therapists

Coutard reported cures but also described reactions of the skin and mucosa showing that they depended for specific doses on the total duration of treatment

History

Evolution of "Standard" Fractionation Schedules

In 1937 Baclesse took over from Coutard in the Curie Institute. He further extended treatment time to avoid the severe reactions seen by Coutard, limiting the daily doses to 2 Gy and protracting treatment over 6-7 weeks. Data from patients treated between 1919 and 1947 suggests that the best outcomes were seen in those receiving treatment over this time frame as opposed to longer or shorter time periods. This technique was exported to the USA around this time.

In contrast to this technique were those developed in Manchester by Paterson. Due to the usual pressures the NHS seems to have with beds and equipment, treatment times were shortened to three weeks with a corresponding drop in the total dose to compensate for larger fraction sizes. This "Manchester" technique was popular in the Commonwealth in contrast to the "Paris" technique popular in continental Europe and the USA.

Rationale of fractionation

- **Sparing of normal tissue**
  - **Repopulation** from surviving fraction
  - **Repair** of sublethal damage
- **Increase tumor damage**
  - **Reoxygenation** of hypoxic cells
  - **Redistribution** of cells along cell cycle

The 4 Rs of radiobiology

Improved Therapeutic

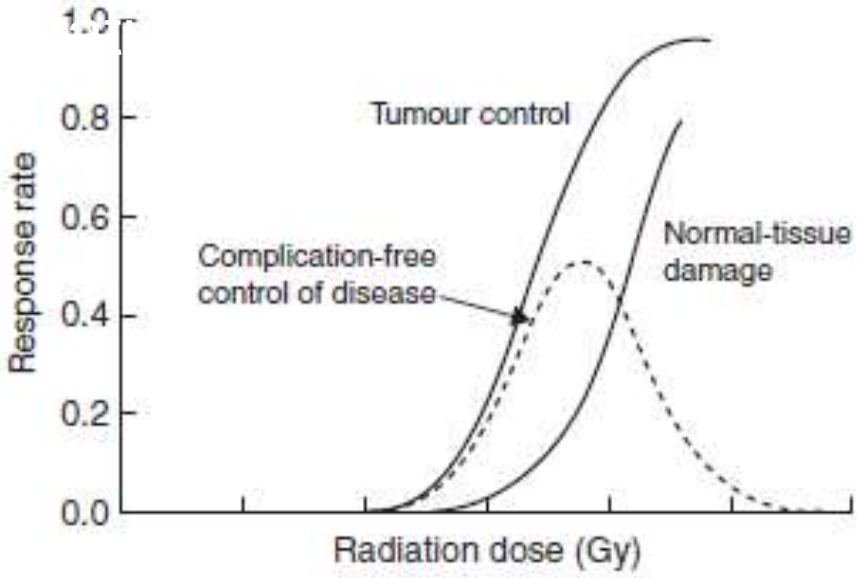


Figure 10.1 Dose–response curves for tumour control and normal-tissue damage. The uncomplicated local tumour control rate initially increases with increasing dose after which it falls again because of a steep increase in the incidence of damage to normal tissue. Adapted from Holthusen (1936).

Fractionation

Standard / Conventional Fractionation

Altered / Modified Fractionation

- Hyper Fractionation
- Accelerated Fractionation
- Continuous Hyperfractionated Accelerated Radiation Therapy (CHART)
- Hypofractionation
- Split Course Radiotherapy
- Concomitant Boost
- SIB

STANDARD FRACTIONATION

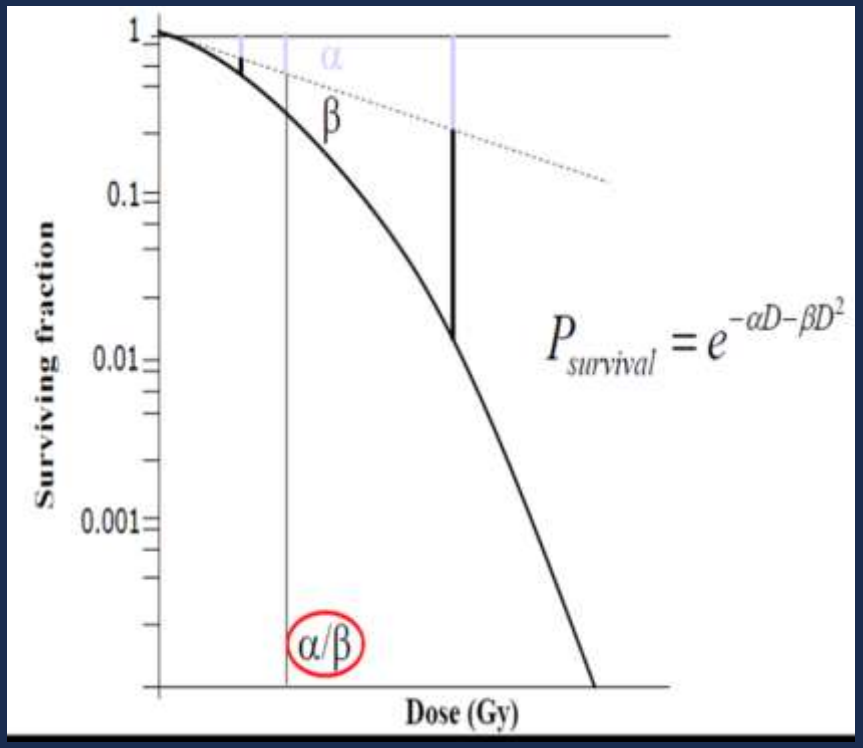
- 1.8 Gy to 2.0 Gy per # daily
- Single # per day
- Five fractions a week.
- Total dose – 50-70 Gy
- Total time – 5-7wks
- Empirical basis. (Fletcher,1988)

Altered Fractionation - Rationale

Linear-quadratic [α/β] model

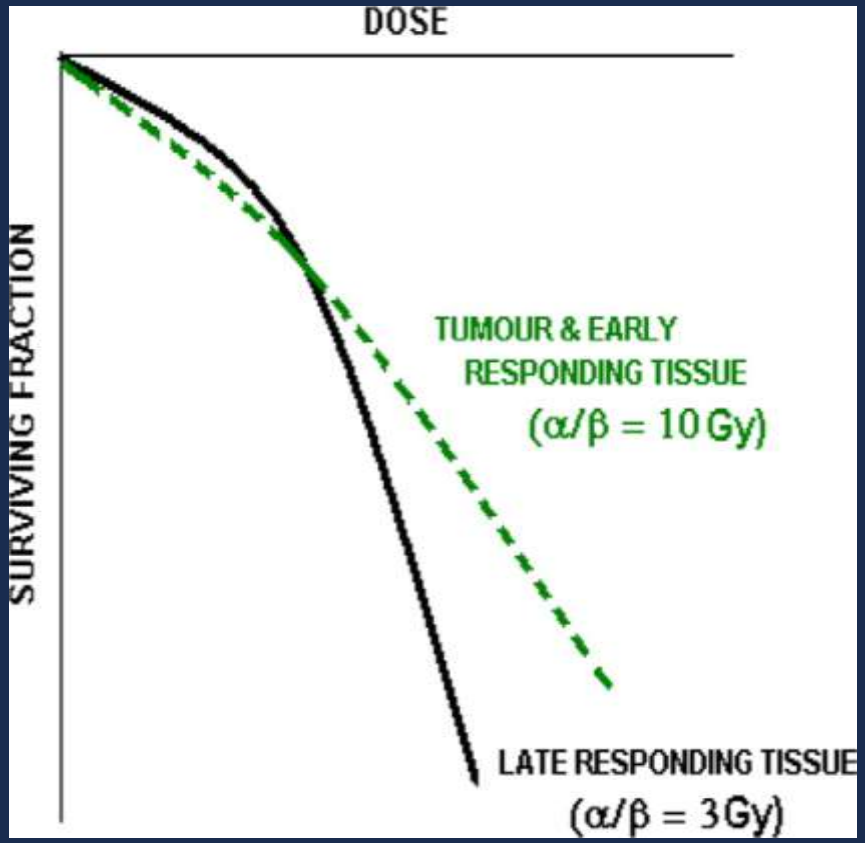
cell injury mechanism is largely regulated by

- **Coefficient α- lethal single impact injury**
- **Coefficient β-lethal injury due to accumulation of sub-lethal injuries**
- **α/β ratio (intersection) gives a dose at which α-component equals β-component.**



Large vs small [α/β] ratios

- Large [α/β] typical of tumors means low sensitivity to change in dose per fraction
- Small [α/β] ratio typical of late sequlae means high sensitivity to changes in dose per fraction.



comparison

HIGH a/β]

- Rapidly proliferating
- a/β more than 5
- Short doubling time(Tpot) HNSCC 4.5d
- Repopulate on treatment
- Sensitive to rate of dose accumulation , OTT
- Short latent period
- Hyper#/acceleration

LOW a/β

- Slow proliferation
- a/β less than 5
- Longer Tpot, breast 10.4d
- No repopulation on treat
- Sensitive to dose /# and inter# time
- Longer latent period
- Hypo#

Choice of fractionation

- If α/β ratio of tumor is the same or less than that of the critical normal tissue, then a larger dose per fraction *(hypofractionation)* is preferred.

i.e., prostate cancer, breast cancer

Brenner D., IJROBP 57: 912-914, 2003

- If α/β ratio of tumor is high (often 10 or greater) and > α/β ratio of normal tissue (often < 5) a lower dose per fraction *(hyperfractionation)* is preferred.

i.e., squamous cancer of head and neck

Horiot J., Radiother Oncol 25: 231-241, 1992

Altered fractionation

HYPERFRACTIONATION

- -More than one small # per day
- spare late effects
- improves tumor control through redistribution and reoxygenation

ACCELERATED FRACTIONATION

- Reduction of treatment time
- To overcome repopulation
- Late effect not expected to change

HYPOFRACTIONATION

- Delivers large dose per #
- Concerns late effects

Hypofractionation

T1/T2 N0 Glottic Carcinoma

Recommendations

63 Gy in 28 fractions over 5.5 weeks (Grade B)
50 Gy in 16 fractions over 3 weeks (T1 disease only) (Grade C)
55 Gy in 20 fractions over 4 weeks (Grade C)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based medicine.[10]

Ultra hypofractionation

The American Society for Radiation Oncology (ASTRO), American Society of Clinical Oncology (ASCO), and American Urological Association (AUA) hypofractionation guideline defines moderate hypofractionation as 2.4–3.4 Gy/fraction and ultrahypofractionated radiotherapy as doses per treatment of 5.0 Gy/fraction or higher, thus leaving a “grey zone” between 3.4 and 5 Gy.

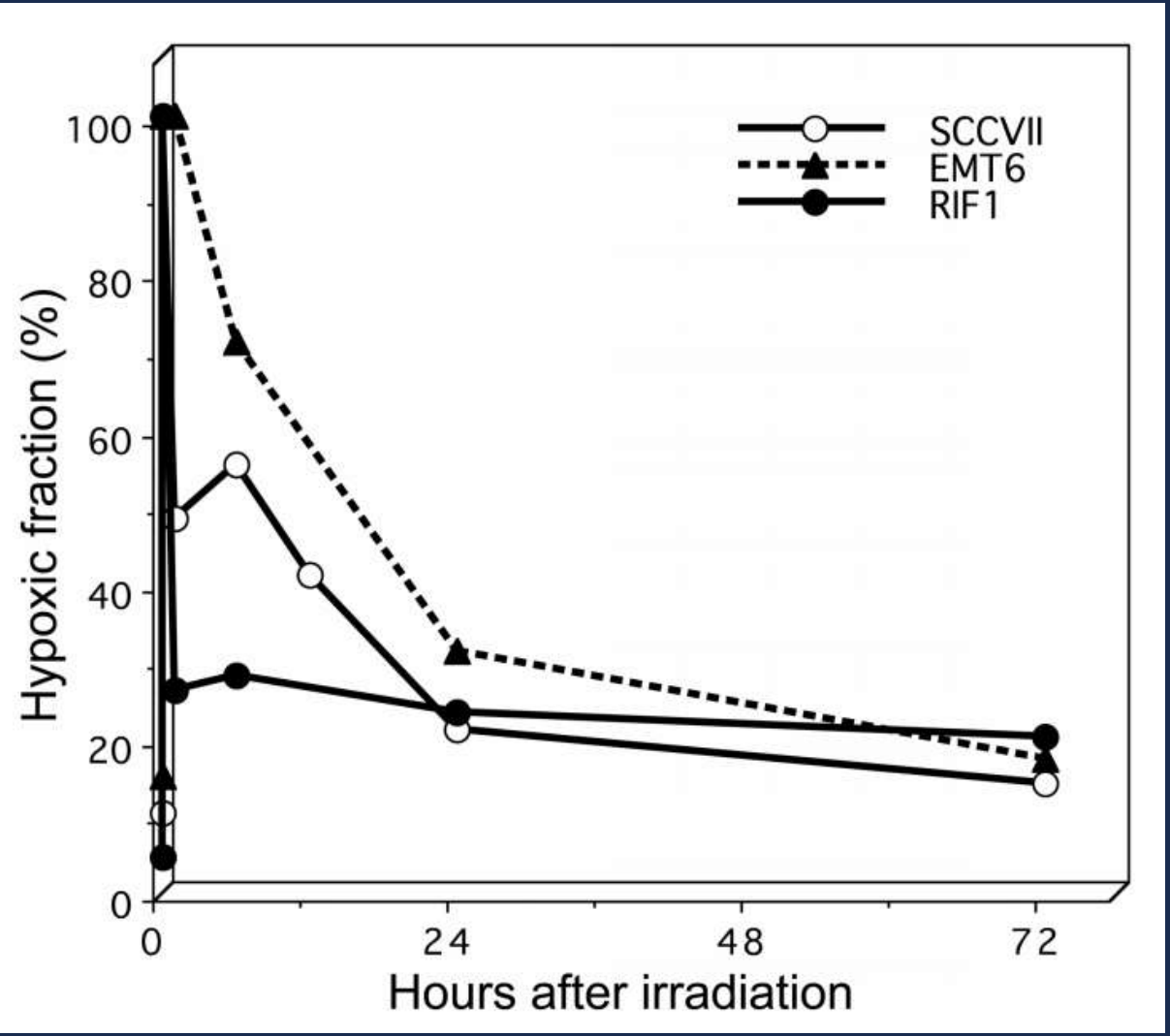
Phenomena influencing effects of high doses per fraction

Vascular damage at high doses and secondary cell killing

Enhanced antitumor immunity after tumor irradiation

In metastatic melanoma patients, SRT of a tumor was reported to contribute to the immunologic rejection of a metastatic lesion at a distant site

ReOxygenation



APPLICABILITY OF THE LQ MODEL TO HYPOFRACTIONATED SRT

Current controversy

Other models offering an alternative to the LQ model
Since it is becoming clearer that LQ formalism is not adequate for
SRT, other models have been proposed.

. Universal survival curve model

, The LQL model (or modified LQ model),

The generalized LQ (gLQ) model

Clinical use of Ultrahypofractionations

Breast

Prostate

Rectum

Kidney

Lung

Liver

Pancreas

Spine

The radiobiology of breast

BJR

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Cite this article as: Yarnold J. Changes in radiotherapy fractionation—breast cancer. Br J Radiol 2018; 92: 20170849.

PUSHING THE FRONTIERS OF RADIOBIOLOGY: A SPECIAL FEATURE IN MEMORY OF SIR OLIVER SCOTT AND PROFESSOR JACK FOWLER: REVIEW ARTICLE

Changes in radiotherapy fractionation—breast cancer

JOHN YARNOLD, FRCR

Division of Radiotherapy and Imaging, The Institute of Cancer Research, London, UK

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E-mail: john.yarnold@icr.ac.uk

Breast cancer is an exception in showing low α/β ratio.

So they are sensitive to high dose per fraction.

Adjusted α/β value for tumor control was estimated to be 3.5 GY

Table 4. Unconfounded estimates of α/β: START-Pilot & START-A Trials[13]

Adverse effects (815 events/2263 pts): α/β = 3.1 Gy [95% CI (2.0–4.2)]
Tumour relapse (349 events/3646 pts): α/β = 3.5 Gy [95% CI (1.2–5.7)]

Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial

Adrian Murray Brunt*, Joanne S Haviland*, Duncan A Wheatley, Mark A Sydenham, Abdulla Alhasso, David J Bloomfield, Charlie Chan, Mark Churn, Susan Cleator, Charlotte E Coles, Andrew Goodman, Adrian Harnett, Penelope Hopwood, Anna M Kirby, Cliona C Kirwan, Carolyn Morris, Zohal Nabi, Elinor Sawyer, Navita Somaiah, Liba Stones, Isabel Syndikus, Judith M Bliss†, John R Yarnold†, on behalf of the FAST-Forward Trial Management Group

Published Online
April 28, 2020

The lancet

97 hospitals (47 radiotherapy
centres and 50 referring hospitals) in the UK. Patients aged at least 18 years with invasive carcinoma of the breast (pT1–3, pN0–1, M0) after breast conservation surgery or mastectomy were eligible.

Between Nov 24, 2011, and June 19, 2014, we recruited and obtained consent from 4096 patients from 97 UK centres,

Interpretation :26 Gy in five fractions over 1 week is non-inferior to the standard of 40 Gy in 15 fractions over 3 weeks for local tumour control, and is as safe in terms of normal tissue effects up to 5 years for patients prescribed adjuvant local radiotherapy after primary surgery for early-stage breast cancer

Int. J. Radiation Oncology Biol. Phys., Vol. 67, No. 4, pp. 1099–1105, 2007

0360-3016/07/$–see front matter

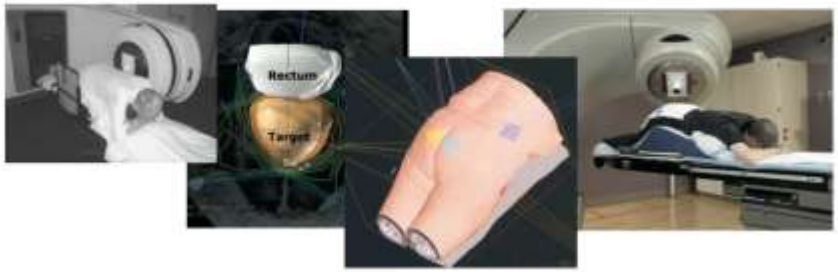
doi:10.1016/j.ijrobp.2006.10.050

CLINICAL INVESTIGATION **Prostate**

STEREOTACTIC HYPOFRACTIONATED ACCURATE RADIOTHERAPY OF THE PROSTATE (SHARP), 33.5 GY IN FIVE FRACTIONS FOR LOCALIZED DISEASE: FIRST CLINICAL TRIAL RESULTS

BERIT L. MADSEN, M.D.,* R. ALEX HSI, M.D.,* HUONG T. PHAM, M.D.,*
JACK F. FOWLER, D.SC., PH.D.,† LAURA ESAGUI, C.M.D.,* AND JOHN CORMAN, M.D.‡

*Sections of Radiation Oncology and ‡Urology, Virginia Mason Medical Center, Seattle, WA; †Emeritus, Department of Human Oncology, Medical School, University of Wisconsin, Madison, WI



SBRT DOSE SCHEDULES

Dose ranges:	BED (α/β=2)	
6.70 x 5 = 33.5 Gy	146	Madsen IJROBP 2007
7.25 x 5 = 36.25 Gy	168	
7.5 x 5 = 37.5 Gy	178	
9.0 x 4 = 36.0 Gy	198	Fuller IJROBP 2008
8.0 x 5 = 40.0 Gy	200	King RO 2013 Meier TCR 2014 Mantz FO 2014
9.0 x 5 = 45.0 Gy	248	
9.5 x 5 = 47.5 Gy	273	Kim IJROBP 2014
10.0 x 5 = 50.0 Gy	300	
24 x 1 = 24 Gy	312	Greco, Lisbon

King IJROBP 2009
King IJROBP 2011
Friedland TCRT 2009
Katz BMC Urol 2010
Wiegner IJROBP 2010
Bolzicco TCRT 2010
Aluwini J Endourol 2010
Freeman RO 2010
Townsend AJCO 2011
Kang Tumori 2011
Jabbari IJROBP 2011
Chen RO 2013

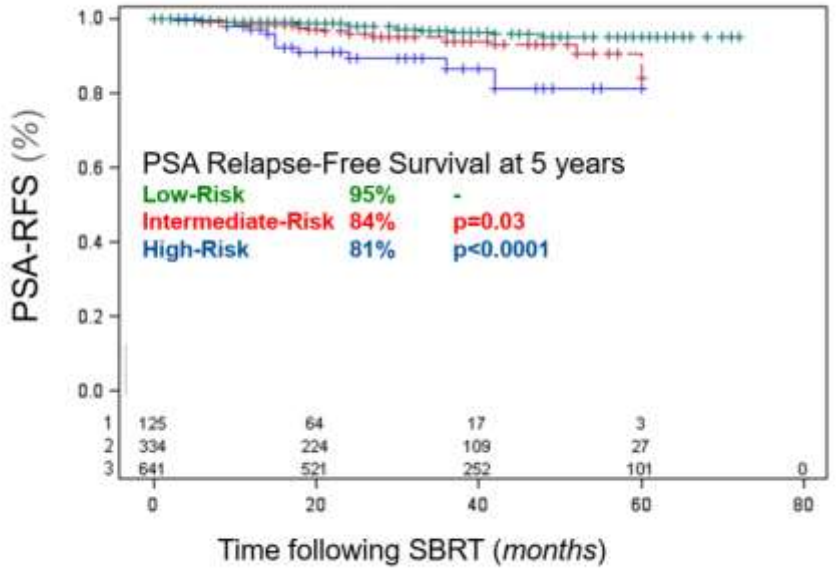
BED equivalent to LDR or HDR prostate RT

Prostate SBRT Consortium Pooled Data

- Pooled database: 1100 patients (2012)
  - Follow PSA profiles / QOL data
  - **Not a meta-analysis**
- 8 institutions (US & international)
- Prospective phase II trials
- Median follow-up: 3 years (1 to 7+ yrs)

CR King, et al. Radiotherapy & Oncology (2013) 109:217-21

Disease-free Survival after SBRT



CR King, et al. Radiotherapy & Oncology (2013) 109:217-21

RANDOMIZED SBRT TRIALS

	SBRT Arm		Arm 2
•RTOG 0938:	Small trial – QOL endpoint 36.25 at 7.25 Gy 5 fractions	vs	51.6 at 4.3 Gy 12 fractions
•PCG GU 002: Protons, N=82	38 at 7.6 Gy 5 fractions	vs	79.2 at 1.8 Gy 44 fractions
•U Miami Heat:	31.25 at 6.25 Gy 5 fractions	vs	70.2 at 2.6 Gy 26 fractions
•HYPO-RT-PC: N=592	42.7 at 6.1 Gy 7 fractions	vs	78 at 2 Gy 39 fractions
•PACE trial:	36.25 at 7.25 Gy 5 fractions	vs	78 at 2Gy 39 fractions

Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial

Anders Widmark, Adalsteinn Gunnlaugsson, Lars Beckman, Camilla Thellenberg-Karlsson, Morten Hoyer, Magnus Lagerlund, Jan Kindblom, Claes Ginman, Bengt Johansson, Kirsten Björnlinger, Mihajl Seke, Måns Agrup, Per Fransson, Björn Tavelin, David Norman, Björn Zackrisson, Harald Anderson, Elisabeth Kjellén, Lars Franzén, Per Nilsson

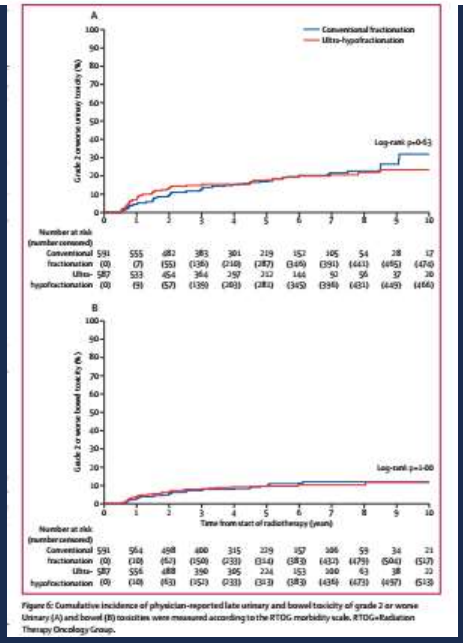


Figure 6: Cumulative incidence of physician-reported late urinary and bowel toxicity of grade 2 or worse
Urinary (A) and bowel (B) toxicities were measured according to the RTOG morbidity scale. RTOG=Radiation Therapy Oncology Group.

1200 patients

Interpretation Ultra-hypofractionated radiotherapy is non-inferior to conventionally fractionated radiotherapy for intermediate-to-high risk prostate cancer regarding failure-free survival. Early side-effects are more pronounced with ultra-hypofractionation compared with conventional fractionation whereas late toxicity is similar in both treatment groups. The results support the use of ultra-hypofractionation for radiotherapy of prostate cancer.

PACE TRIAL

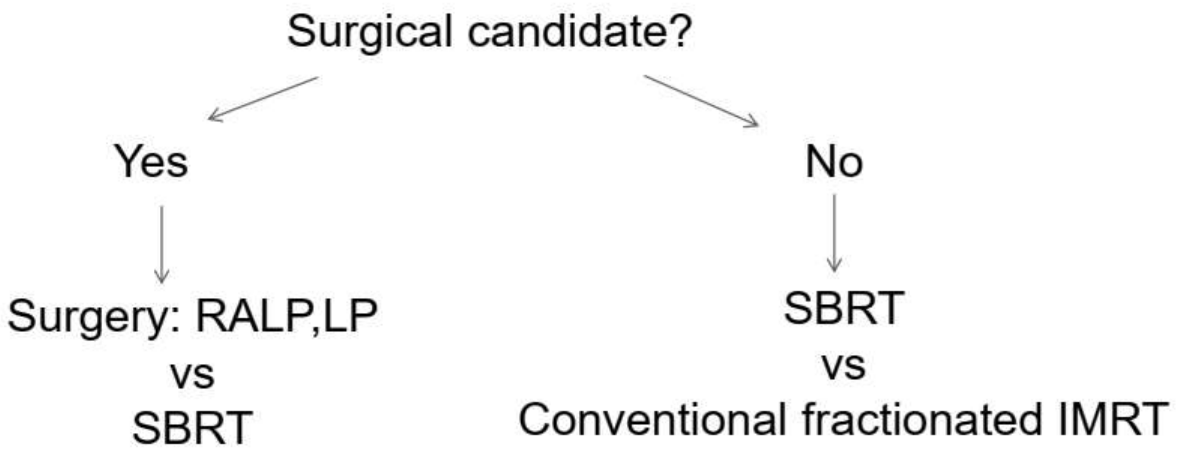
Randomized trial. UK. N=1716.

LOW AND INTERMEDIATE RISK

PSA < 20 ng/ml

Gleason score ≤ 3 + 4 = 7

Clinical stage T1c -T2c, N0-X, M0-X



PI: N. Van As

UK Clinical Research Network.

Intensity-modulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, non-inferiority trial

Douglas H Brand, Alison C Tree*, Peter Ostler, Hans van der Voet, Andrew Loblaw, William Chu, Daniel Ford, Shaun Tolan, Suneil Jain, Alexander Martin, John Staffurth, Philip Camilleri, Kiran Kancherla, John Frew, Andrew Chan, Ian S Dayes, Daniel Henderson, Stephanie Brown, Clare Cruickshank, Stephanie Burnett, Aileen Duffton, Clare Griffin, Victoria Hinder, Kirsty Morrison, Olivia Naismith, Emma Hall, Nicholas van As, on behalf of the PACE Trial Investigators*

Interpretation Previous evidence (from the HYPO-RT-PC trial) suggested higher patient-reported toxicity with ultrahypofractionation. By contrast, our results suggest that substantially shortening treatment courses with stereotactic body radiotherapy does not increase either gastrointestinal or genitourinary acute toxicity.

Clinical Oncology xxx (2018) 1–6

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Original Article

Early Results of Extreme Hypofractionation Using Stereotactic Body Radiation Therapy for High-risk, Very High-risk and Node-positive Prostate Cancer

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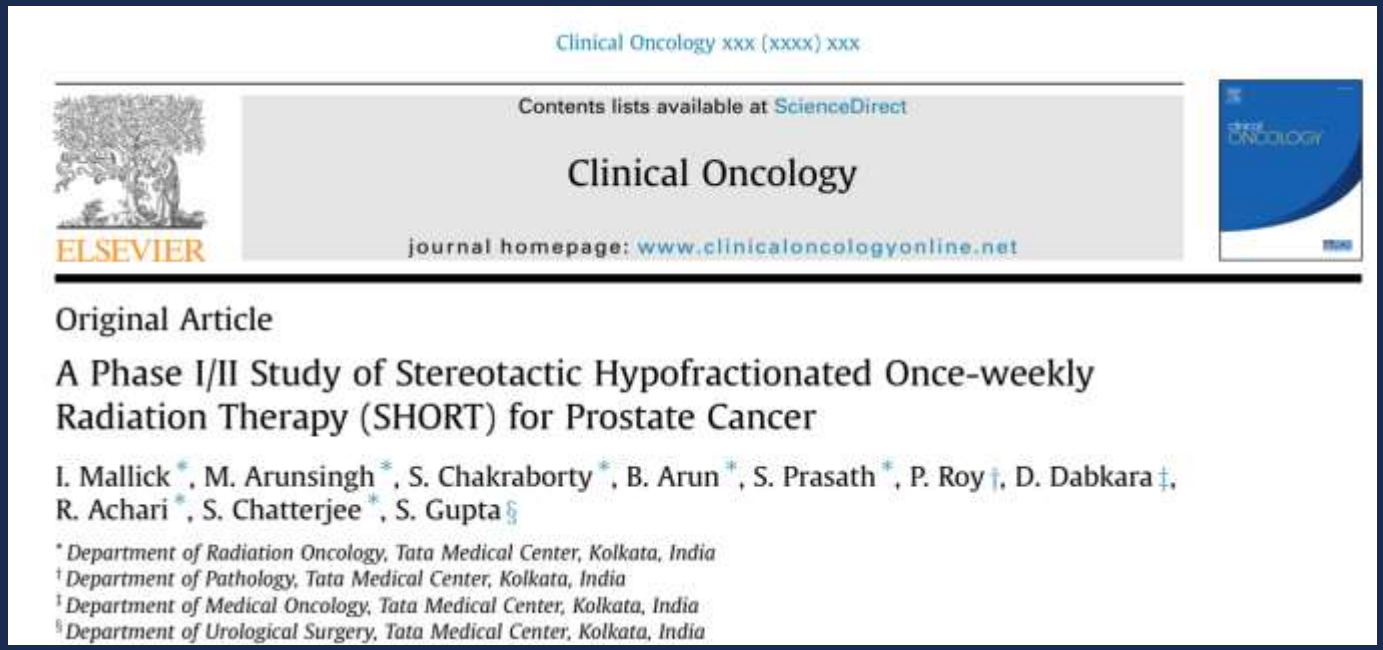
Table 2
Patient characteristics at diagnosis

Age: Median (range)	68 (44–89)	
Clinical T stage		
	T2a	1 (2%)
	T2b	2 (3%)
	T2c	15 (23%)
	T3a	12 (17%)
	T3b	22 (32%)
	T4	16 (23%)
Clinical N stage		
	N0	27 (46%)
	N1	37 (54%)
Risk grouping		
	High risk	20 (29%)
	Very high risk	11 (17%)
	Node positive	37 (54%)
ADT		

Conclusion: SBRT is safe in the treatment of high-risk, very high-risk and node-positive prostate cancer, even with prophylactic pelvic radiotherapy or prior transurethral resection of prostate. Longer follow-up is required to determine efficacy



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Original Article

A Phase I/II Study of Stereotactic Hypofractionated Once-weekly Radiation Therapy (SHORT) for Prostate Cancer

I. Mallick [*], M. Arunsingh [*], S. Chakraborty [*], B. Arun [*], S. Prasath [*], P. Roy [†], D. Dabkara [‡], R. Achari [*], S. Chatterjee [*], S. Gupta [§]

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Conclusion: In a cohort of mainly high-risk cancers, stereotactic once-weekly radiation therapy was easy to implement and well tolerated, with a low incidence of acute and late toxicity and excellent biochemical control.

Short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial

Renu R Bahadoer, Esmée A Dijkstra*, Boudewijn van Etten†, Corrie A M Marijnen†, Hein Putter, Elma Meershoek-Klein Kranenbarg, Annet G H Roodvoets, Iris D Nagtegaal, Regina G H Beets-Tan, Lennart K Blomqvist, Tone Fokstuen, Albert J ten Tije, Jaume Capdevila, Mathijs P Hendriks, Ibrahim Edhemovic, Andrés Cervantes, Per J Nilsson†‡, Bengt Glimelius†‡, Cornelis J H van de Velde†‡, Geke A P Hospers†‡, and the RAPIDO collaborative investigators§*

Pathological complete response			
Yes	120/423 (28%)	57/398 (14%)	<0·0001*
No	303/423 (72%)	341/398 (86%)	..

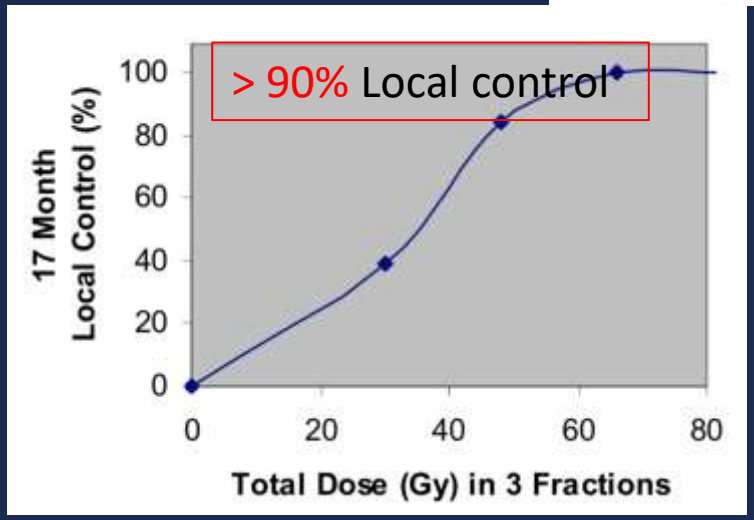
preliminary report

Extracranial Stereotactic Radioablation*

Results of a Phase I Study in Medically Inoperable Stage I Non-small Cell Lung Cancer

Robert Timmerman, MD; Lech Papiez, PhD; Ronald McGarry, MD; Laura Likes, RT; Colleen DesRosiers, MS; Stephanie Frost, MS; and Mark Williams, MD

(CHEST 2003; 124:1946–1955)



RTOG 0236

Stereotactic Body Radiation Therapy for Inoperable Early Stage Lung Cancer

- 3-year Primary tumor control rate: 97.6% ,
- Tumor,involved lobe control rate : 90.6% ; LRC:: 87.2%
- 3-year rate of disseminated failure was 22.1%
- OS at 3 years were 55.8%; Median OS: 48.1 months

SBRT:Standard of Care in Medically Inoperable (stage I, II)

Operable stage I-II, cN0?

- Phase II-RTOG 0618…….96% LC@4yrs
- ROSEL (Dutch)--<=3cm……2008
- STARS (US:Cyberknife) <4cm….. 2008
- RTOG 1021……2010

Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials

Joe Y Chang*, Suresh Senan*, Marinus A Paul, Reza J Mehran, Alexander V Louie, Peter Balter, Harry J M Groen, Stephen E McRae, Joachim Widder, Lei Feng, Ben E E M van den Borne, Mark F Munsell, Coen Hurkmans, Donald A Berry, Erik van Werkhoven, John J Kesti, Anne-Marie Dingemans, Omar Dawood, Cornelis J A Haasbeek, Larry S Carpenter, Katrien De Jaeger, Ritsuko Komaki, Ben J Slotman, Egbert F Smit†, Jack A Roth†

To date, there have been three randomized control trials comparing surgery vs. SBRT in operable patients (ROSEL, STARS, RTOG 1021/ACOSOG Z4099), all of which have closed due to poor accrual. Despite this, a pooled analysis of patients from the STARS and ROSEL trials offers potential insight.

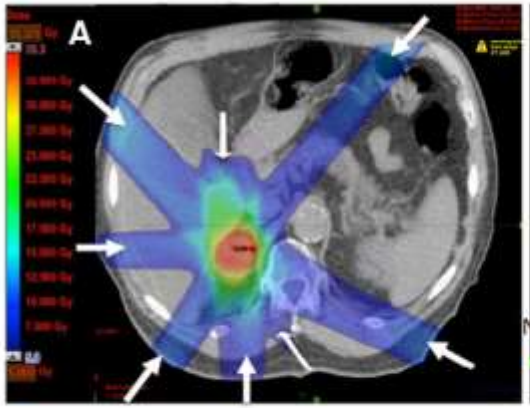
Siva et al. BMC Cancer (2018) 18:1030
https://doi.org/10.1186/s12885-018-4916-2

BMC Cancer

STUDY PROTOCOL Open Access

TROG 15.03 phase II clinical trial of Focal Ablative STereotactic Radiosurgery for Cancers of the Kidney - FASTRACK II

Shankar Siva[1,2*], Brent Chesson[1], Mathias Bressel[1], David Pryor[3], Braden Higgs[4], Hayley M. Reynolds[1], Nicholas Hardcastle[1], Rebecca Montgomery[5], Ben Vanneste[6], Vincent Khoo[7], Jeremy Ruben[8], Eddie Lau[9], Michael S. Hofman[1], Richard De Abreu Lourenco[10], Swetha Sridharan[11], Nicholas R. Brook[5], Jarad Martin[11]



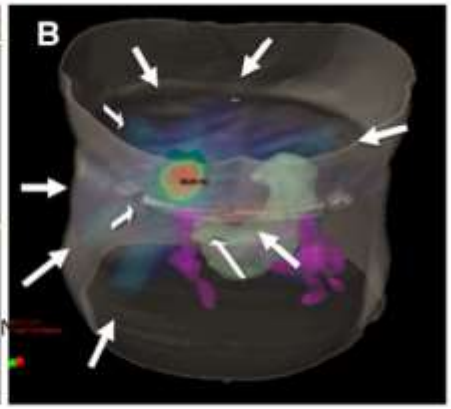


Fig. 1 Axial 3D conformal treatment plan of SABR for right kidney (A) and 3D reconstruction (B) showing multiple beam angles resulting in high-doses wrapping tightly around the target

26Gy/single fraction </=4cm
42Gy/3 fraction >4cm

Local control at 12 months from treatment commencement was 100% (p<0·0001). Seven (10%) patients had grade 3 treatment-related adverse events, with no grade 4 adverse events observed.

Thank you