

Overtreatment by radiotherapy: avoiding late toxicity

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Defining 'Overtreatment'

- More deaths due to RT than prevented by RT
- RT morbidity (rate x severity) outweighs benefits of reduced mortality
- RT morbidity exceeds morbidity of local cancer recurrence

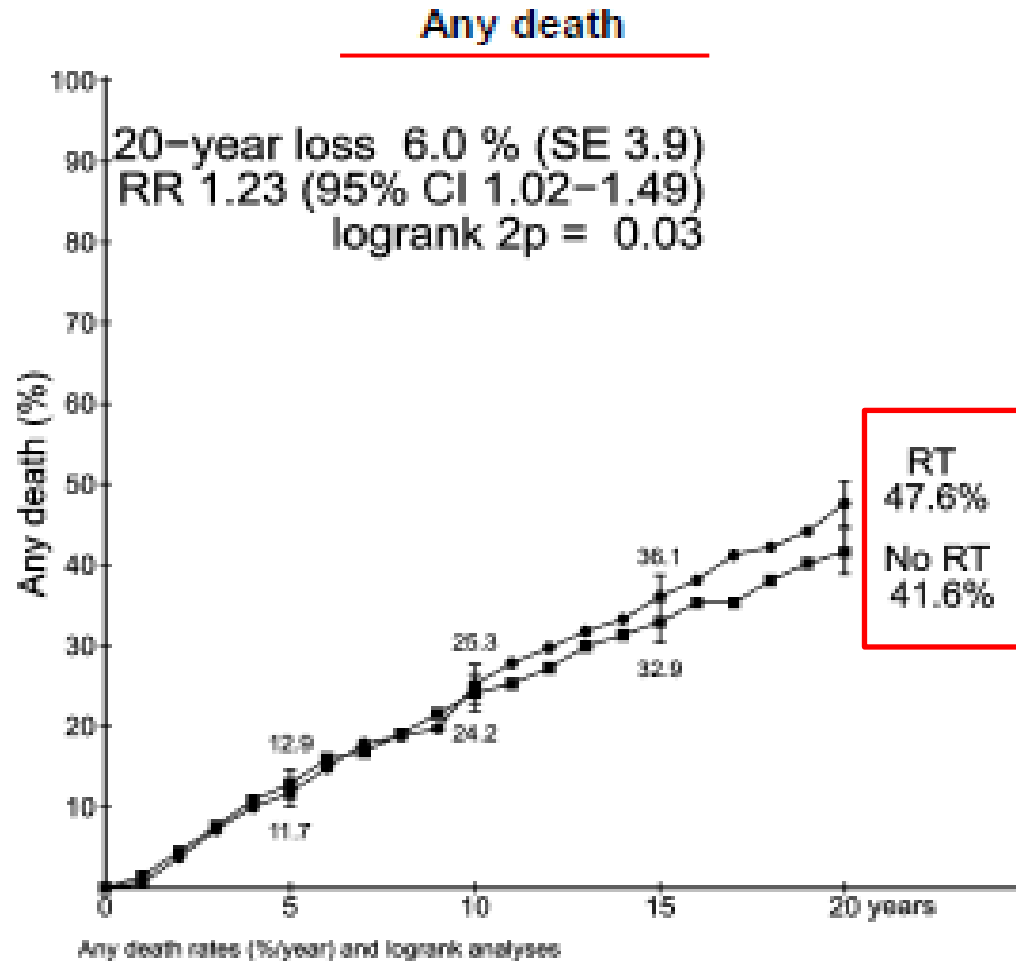
Reducing Overtreatment

- Selective avoidance of RT
 - Low risk populations
 - Low risk anatomical regions
- If needing RT, consider
 - Volumes irradiated
 - Dose intensity

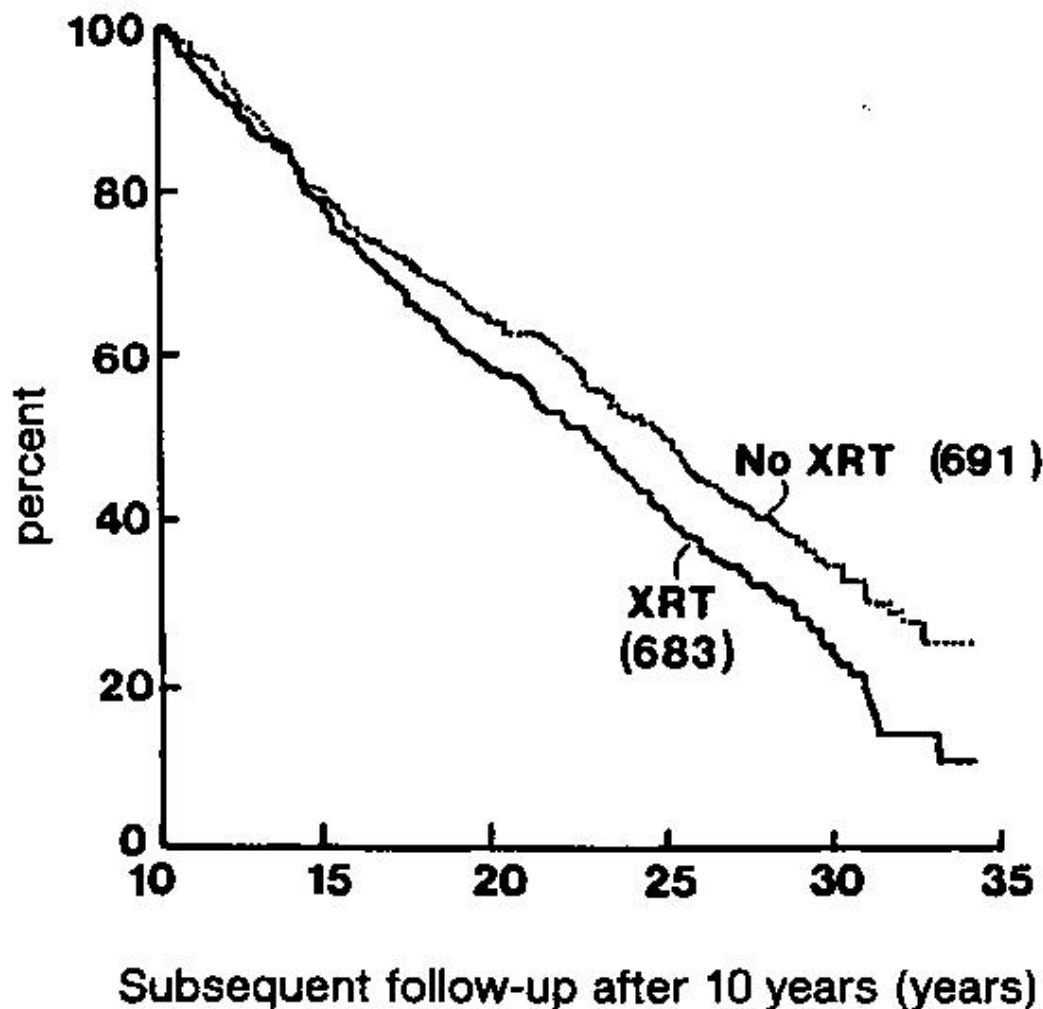
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Excess All-Cause Mortality in pN0 Patients Randomised to Post-Mastectomy RT, 1960-80



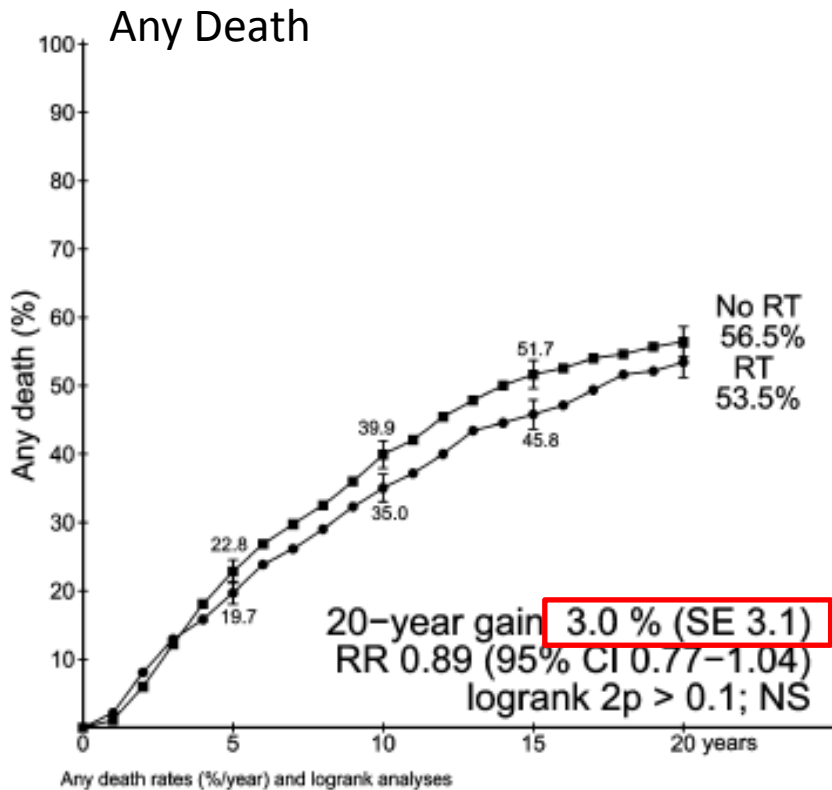
Subsequent Survival in Patients Living 10 Years after Radical Mastectomy +/- Local-Regional RT



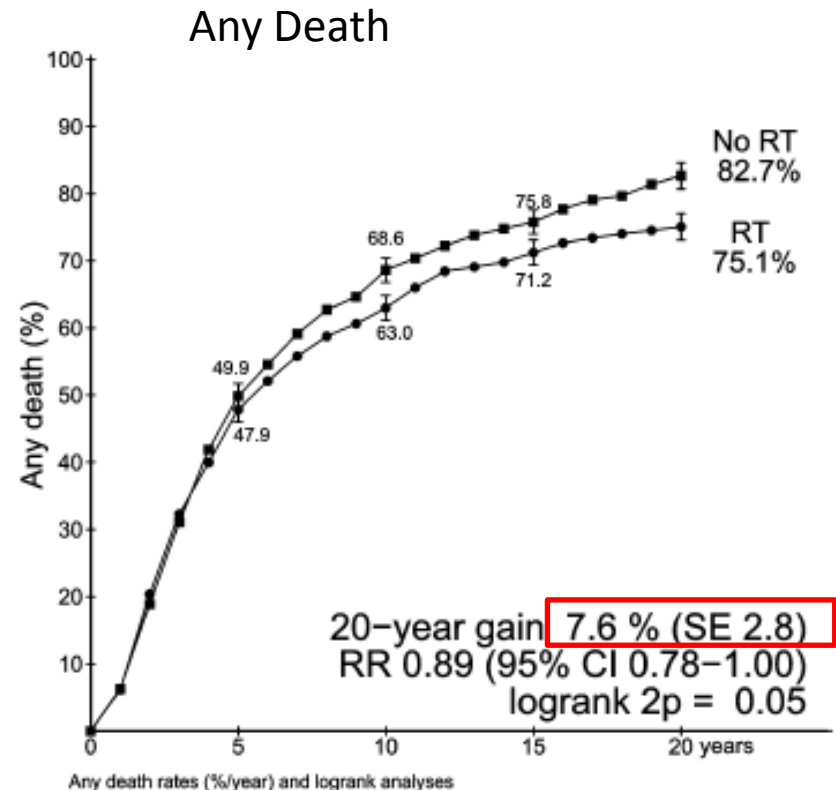
Heart Disease!

All Cause Mortality after Mastectomy + Axillary Dissection + Systemic Therapy \pm RT in pN+ Disease (N=3086)

1-3 metastatic nodes

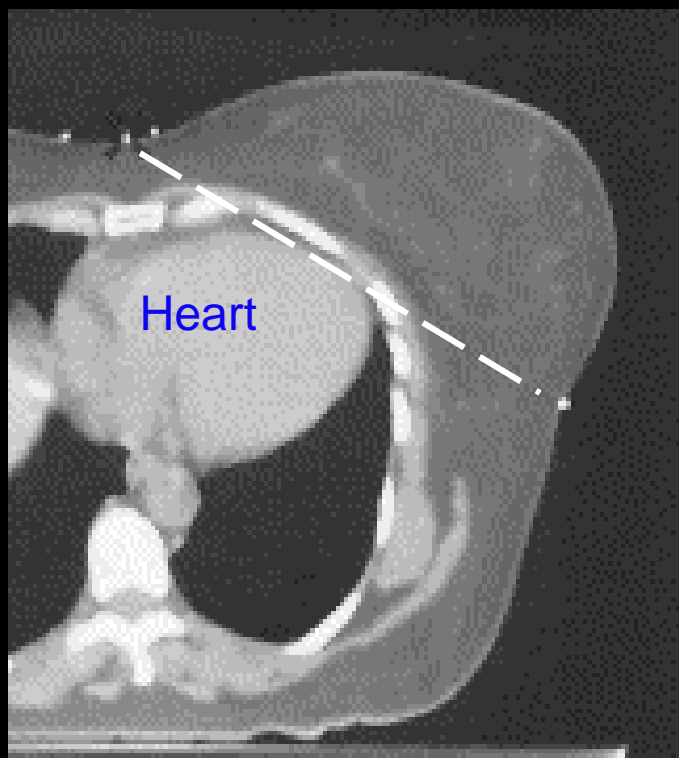


4 or more metastatic nodes

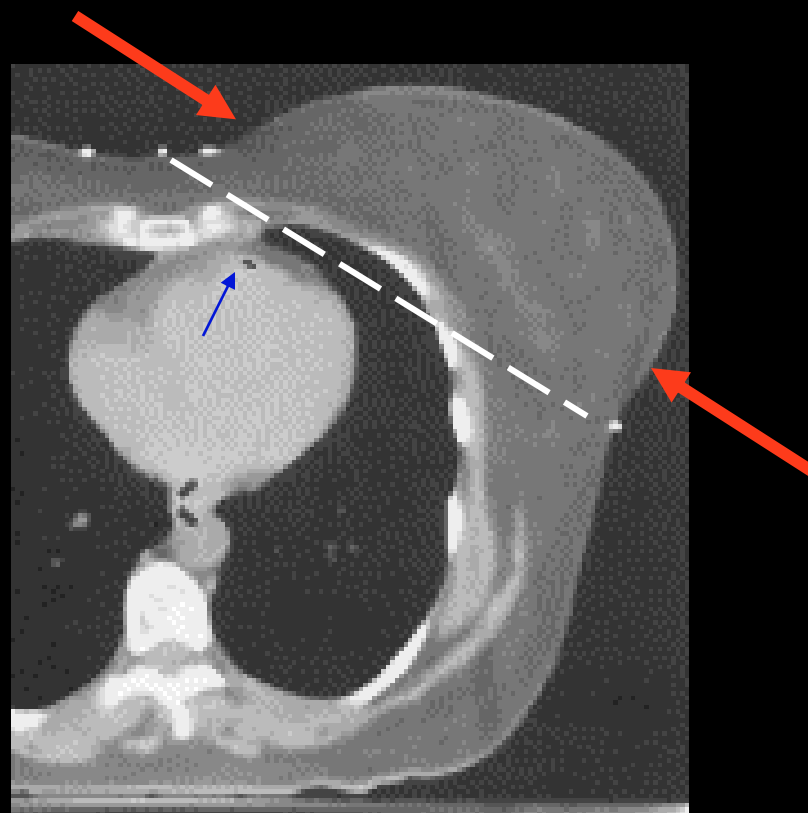


A Deep Breath (hold it for 30 sec) Often gives Full Heart Protection

Expiration:
Beam OFF

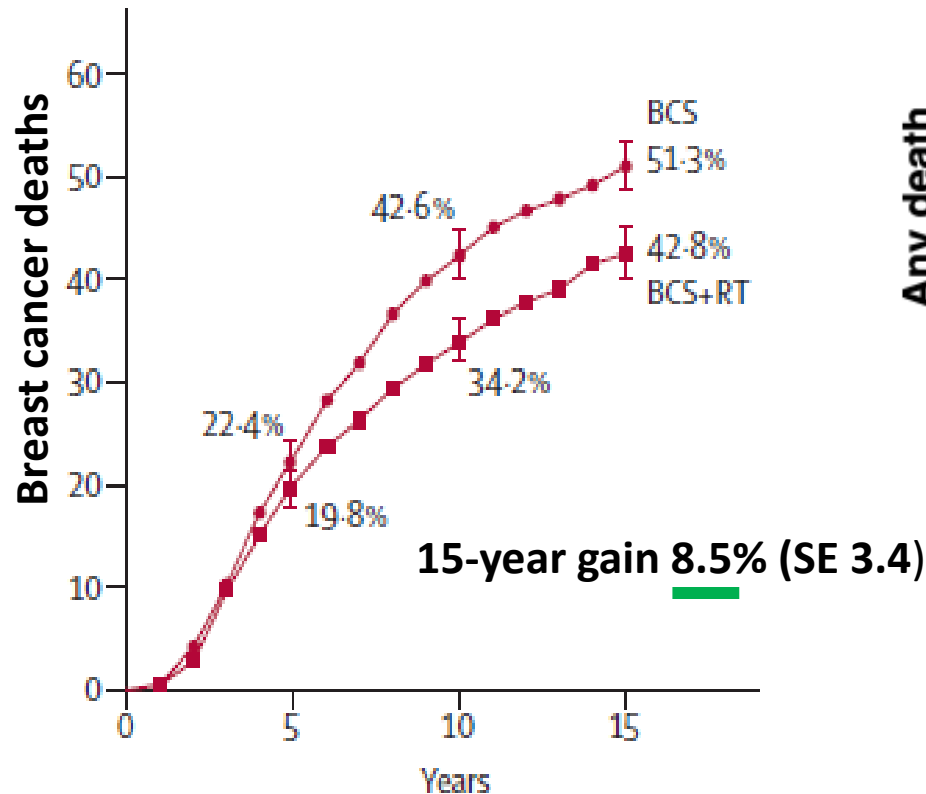


Inspiration:
beams ON

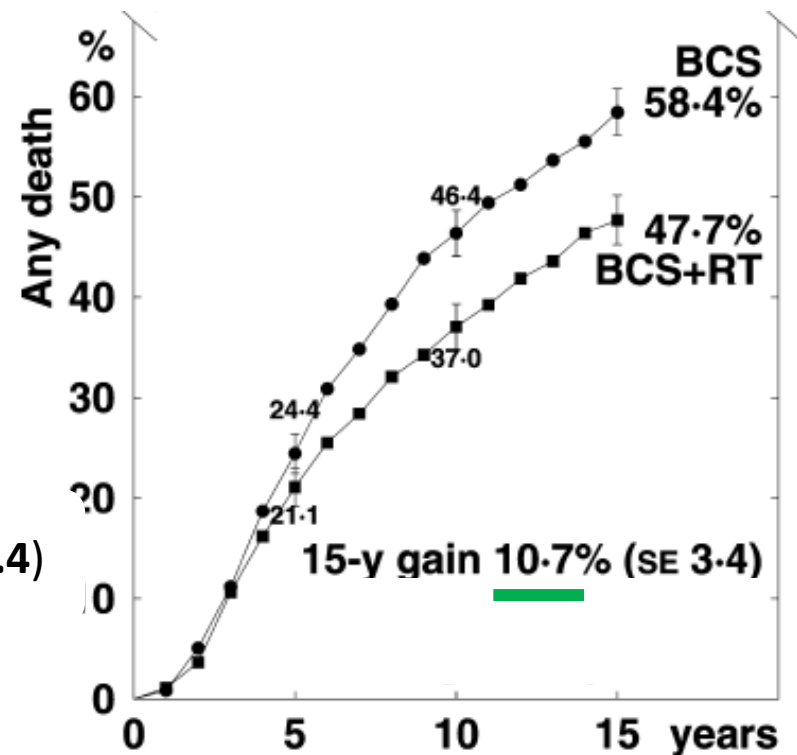


Breast Cancer Deaths in Trials Testing Whole Breast RT after Tumour Excision in Women with Node Metastases, 1980-2000

Breast Cancer Mortality



Any Death

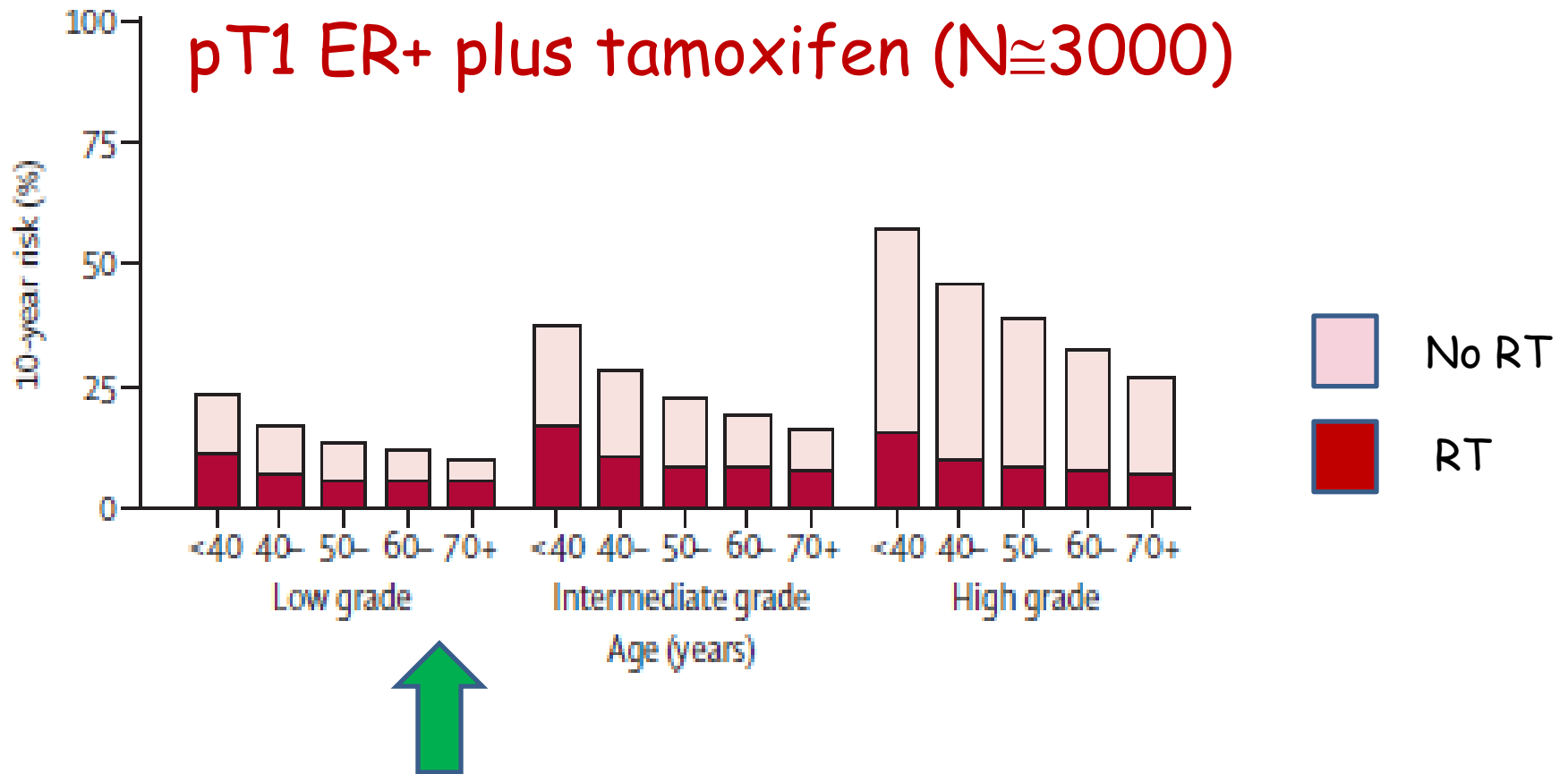


Reducing Risks of Overtreatment

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Should everyone have RT after BCS?

Local Relapse %



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EORTC Trial Testing RT to Internal Mammary Chain

<i>Survival status</i>	No IM-MS (N=2002)	IM-MS (N=2002)
Alive	1573 (78.6)	1620 (80.9)
Death	429 (21.4)	382 (19.1)
<i>Breast cancer</i>	310	259
<i>Other cancer</i>	39	30
<i>Cardiovascular disease</i>	20	22
<i>Toxicity</i>	1	1
<i>Infection</i>	4	8
<i>Other chronic disease</i>	5	3
<i>Other cause</i>	23	25
<i>Unknown</i>	27	34

What are the Implications of ASCOG Z0011 & IBCSG 23-01?

- Ax.Diss. vs No Ax.Diss. in SNB+
- No OS benefit from Ax. Diss. so far
- >90% had BCS + whole breast RT
- Whole breast RT includes many level I/II axillary nodes

Comment: in view of low axillary relapse rates, no reason to modify RT beams

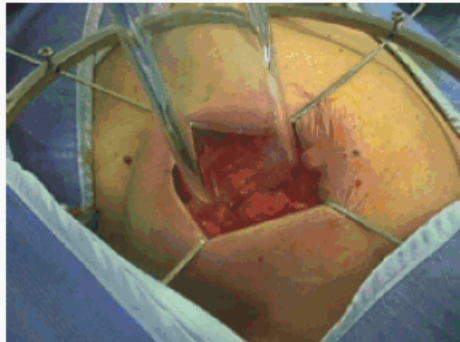
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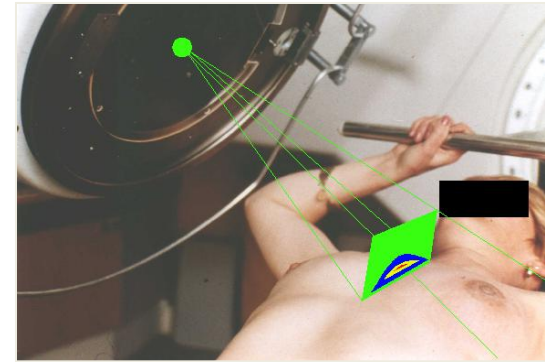
ELIOT Trial (n=1305)

Eligibility: Age > 48yr; T < 25mm

Surgery: Local excision



Randomisation



***IORT**

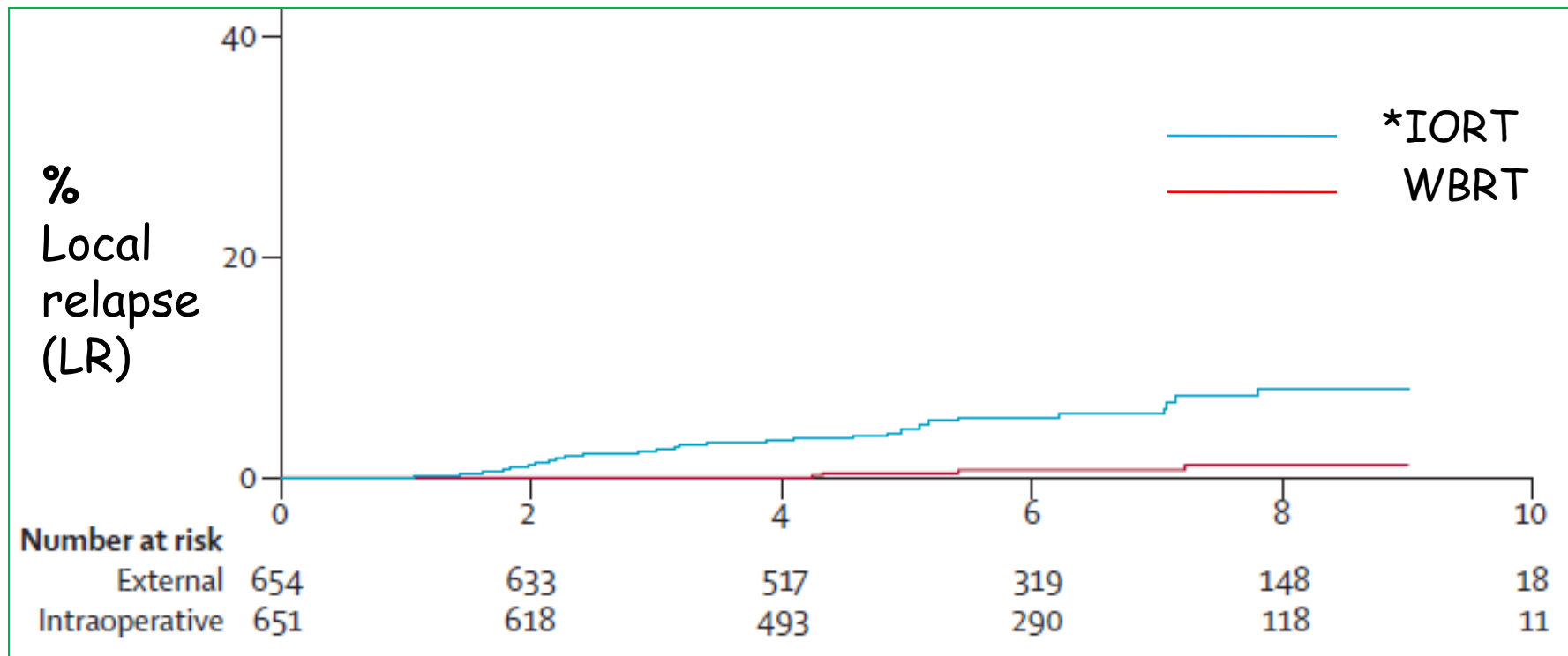
WBRT

21Gy/1F

50Gy/25F WB
10Gy/5F boost

***IORT** = intra-operative RT

ELIOT: Breast Cancer Local Relapse Median FU=6yr



Cumulative LR (%)

Ext RT	0	0	0	0.8	1.3	1.3
ELIOT	0	1.0	3.7	5.9	9.1	11.8

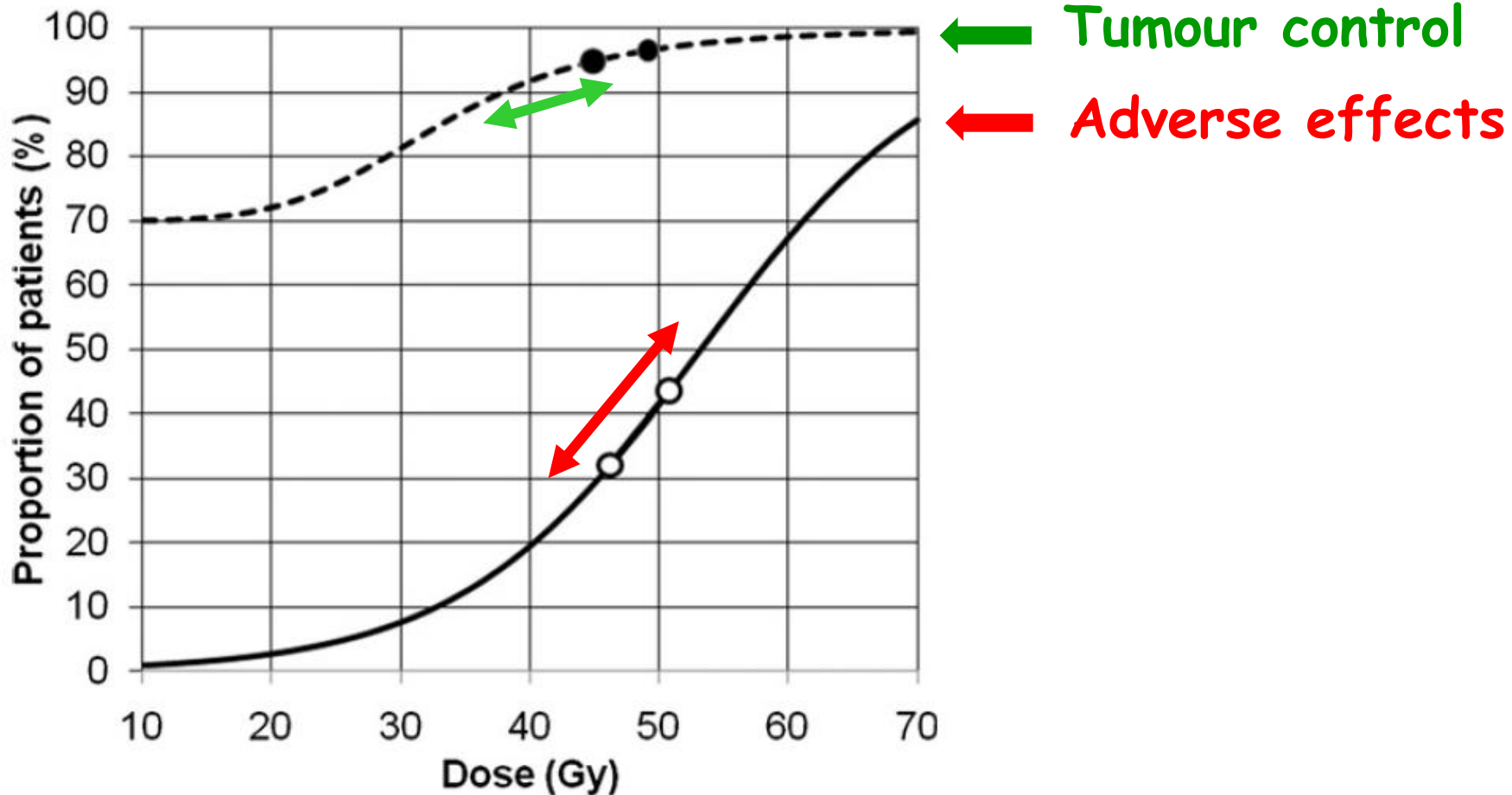
*IORT= intra-operative RT

Orecchia, Lanc Onc, 2013, 14:1269-77

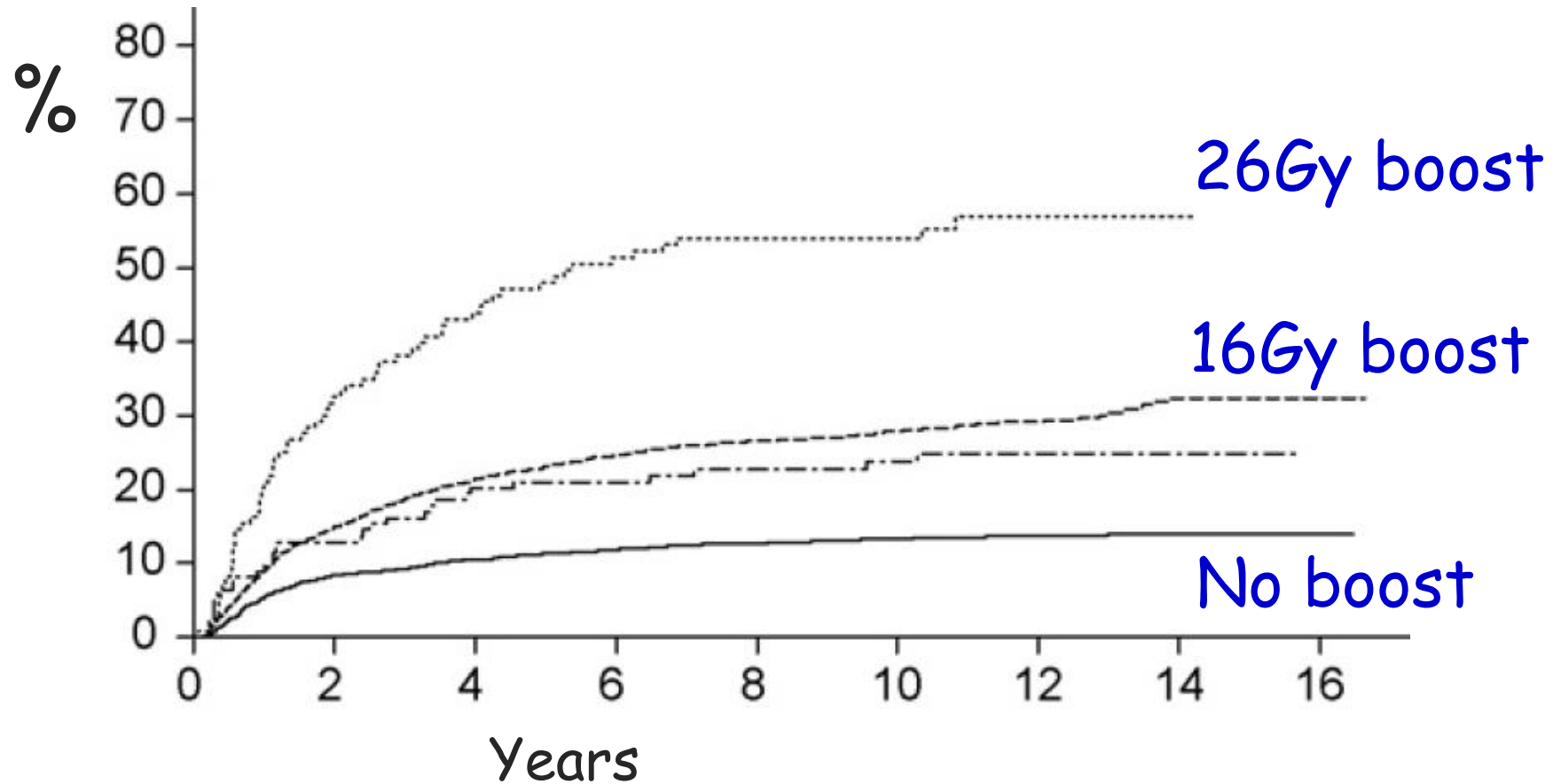
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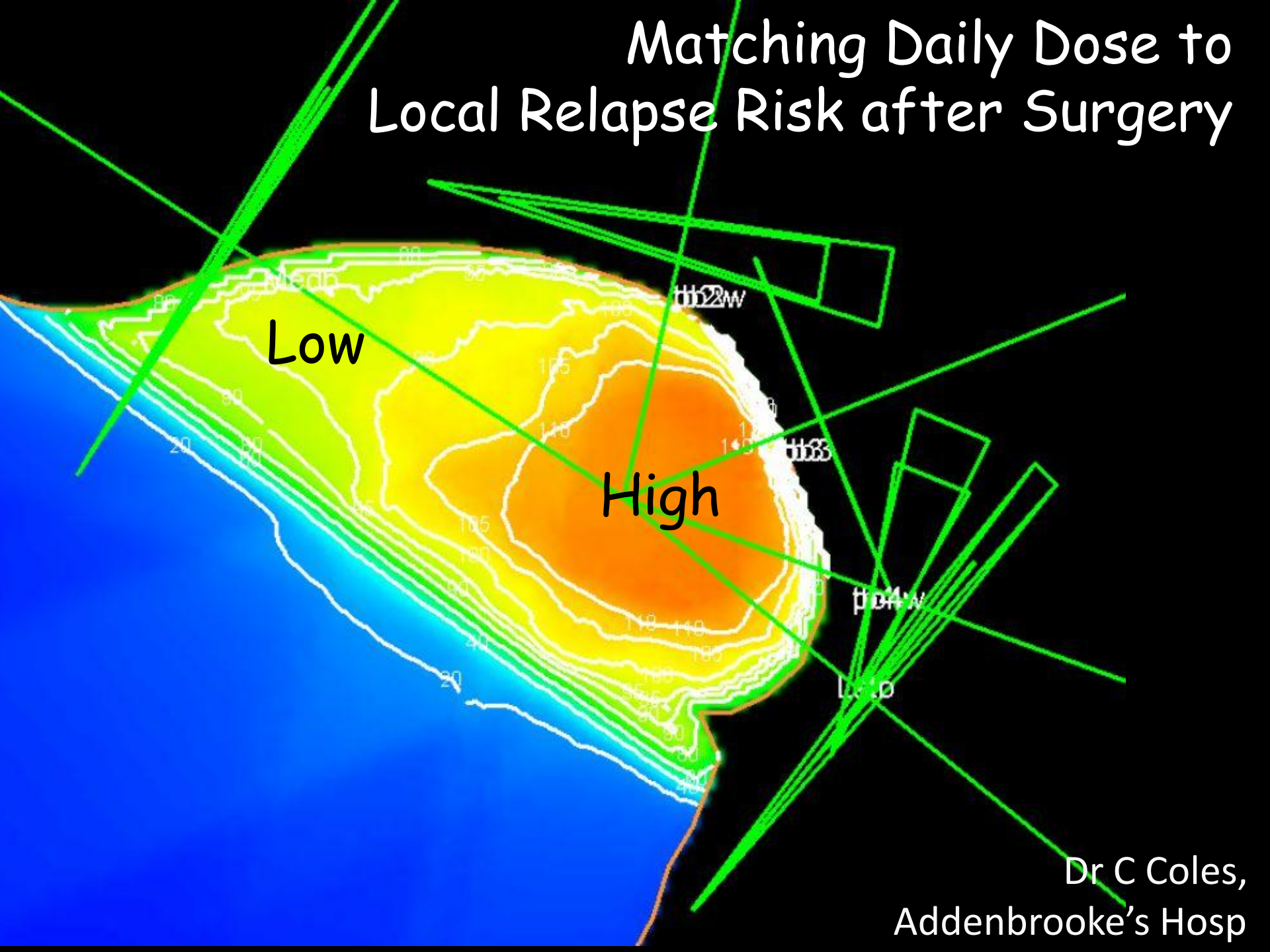
Dose Response for Adverse Effects is Steeper than for Tumour Control



Moderate or Severe Fibrosis in EORTC Boost Trial (N=5318)



Matching Daily Dose to Local Relapse Risk after Surgery

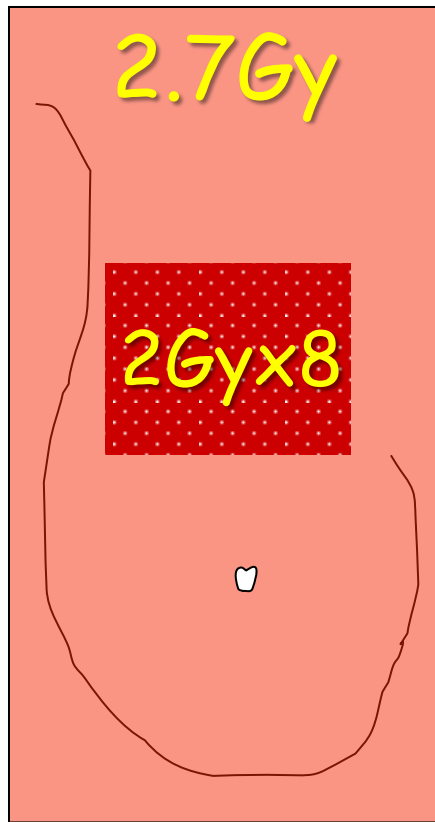


Dr C Coles,

Addenbrooke's Hosp

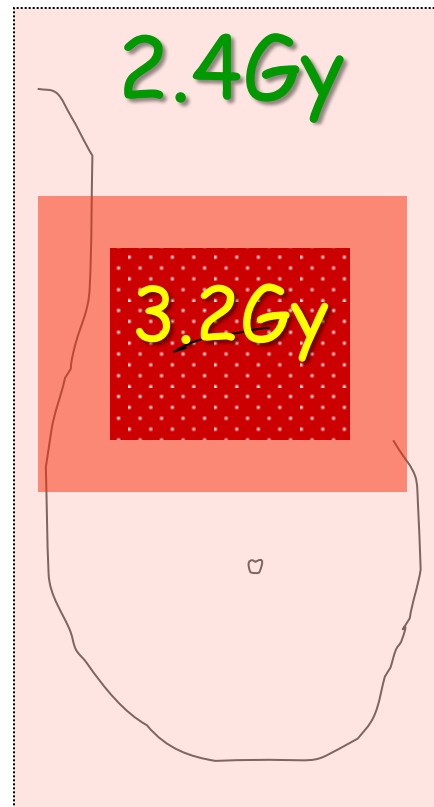
UK IMPORT High Trial (n=2568)

Control
Sequential boost

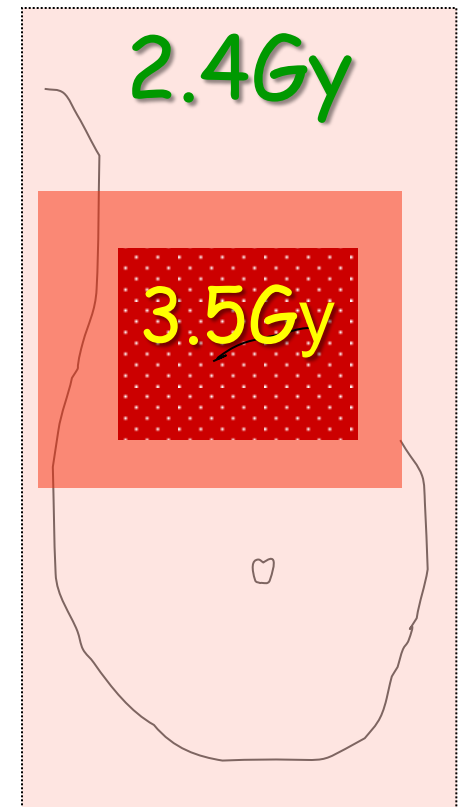


15+8 fractions

Test: Synchronous boost
Group 1 Group 2



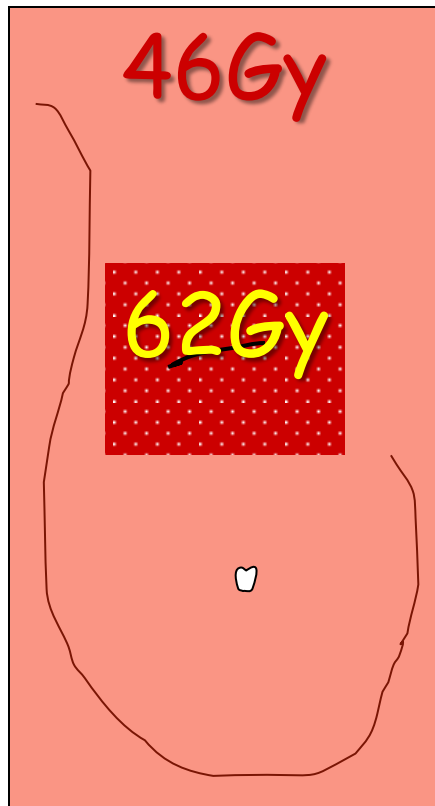
15 fractions



15 fractions

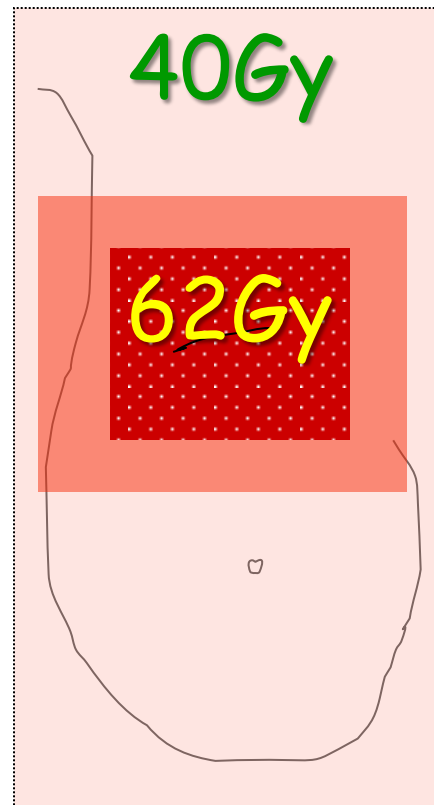
How Do Total Doses Compare to Standard Fractionation, assuming $\alpha/\beta=3\text{Gy}$?

Control



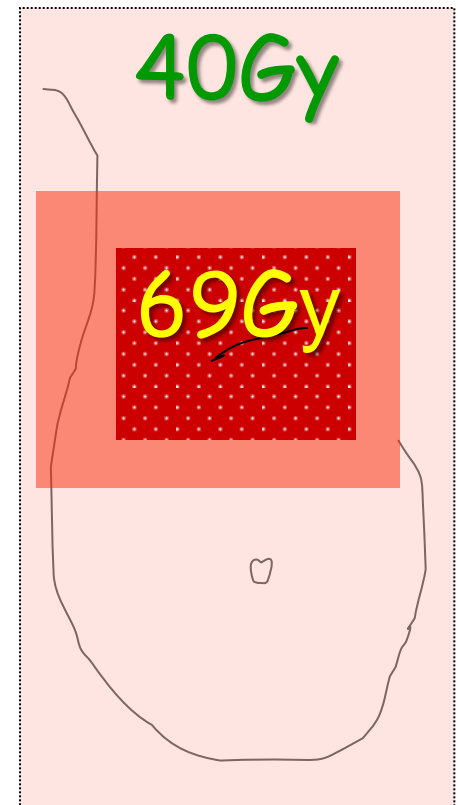
15+8 fractions

Test 1



15 fractions

Test2



15 fractions

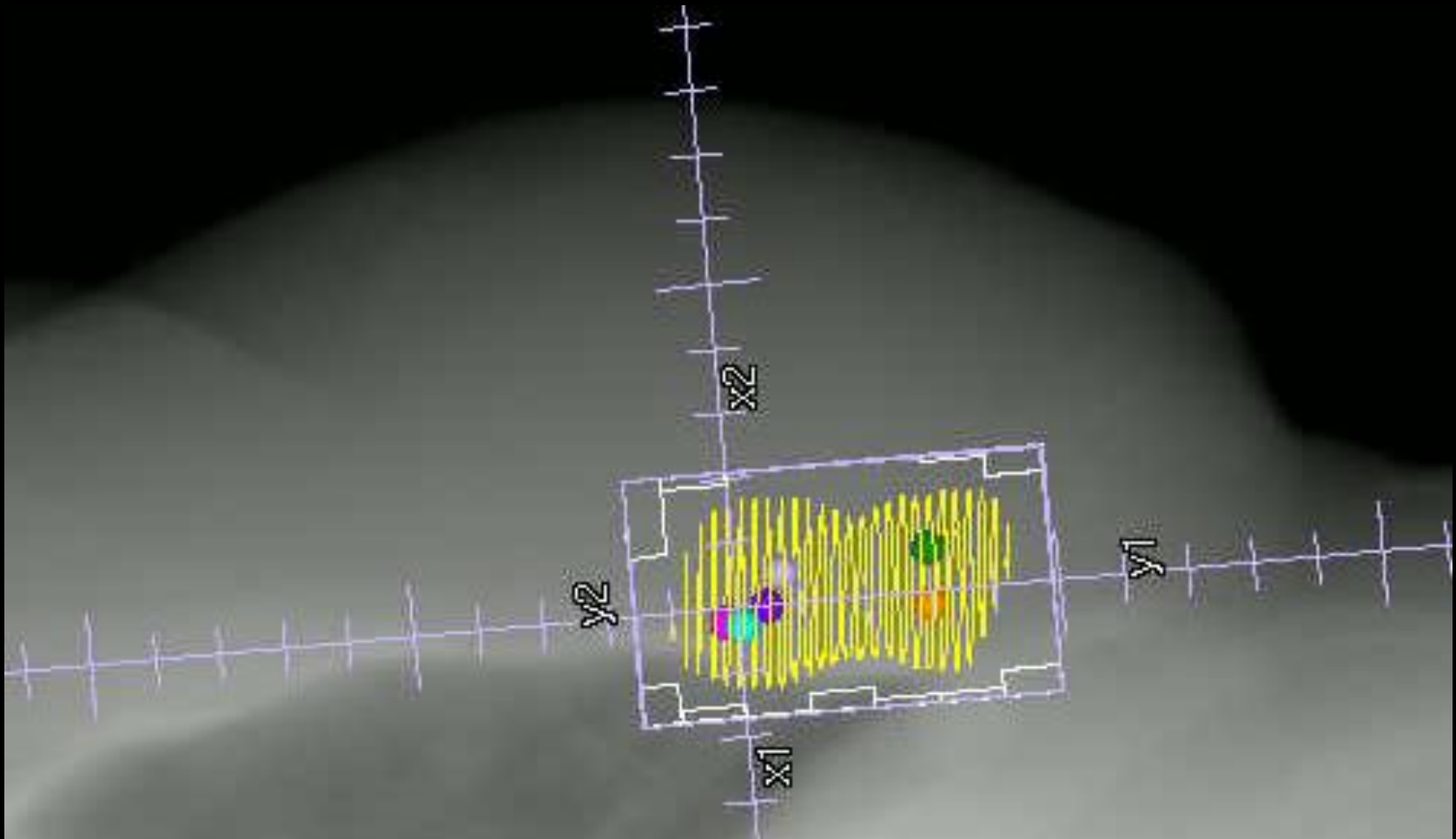
Radiotherapy Checks using a Built-in CT scanner

2. RT beam activated

1. Partial arc
CT scan

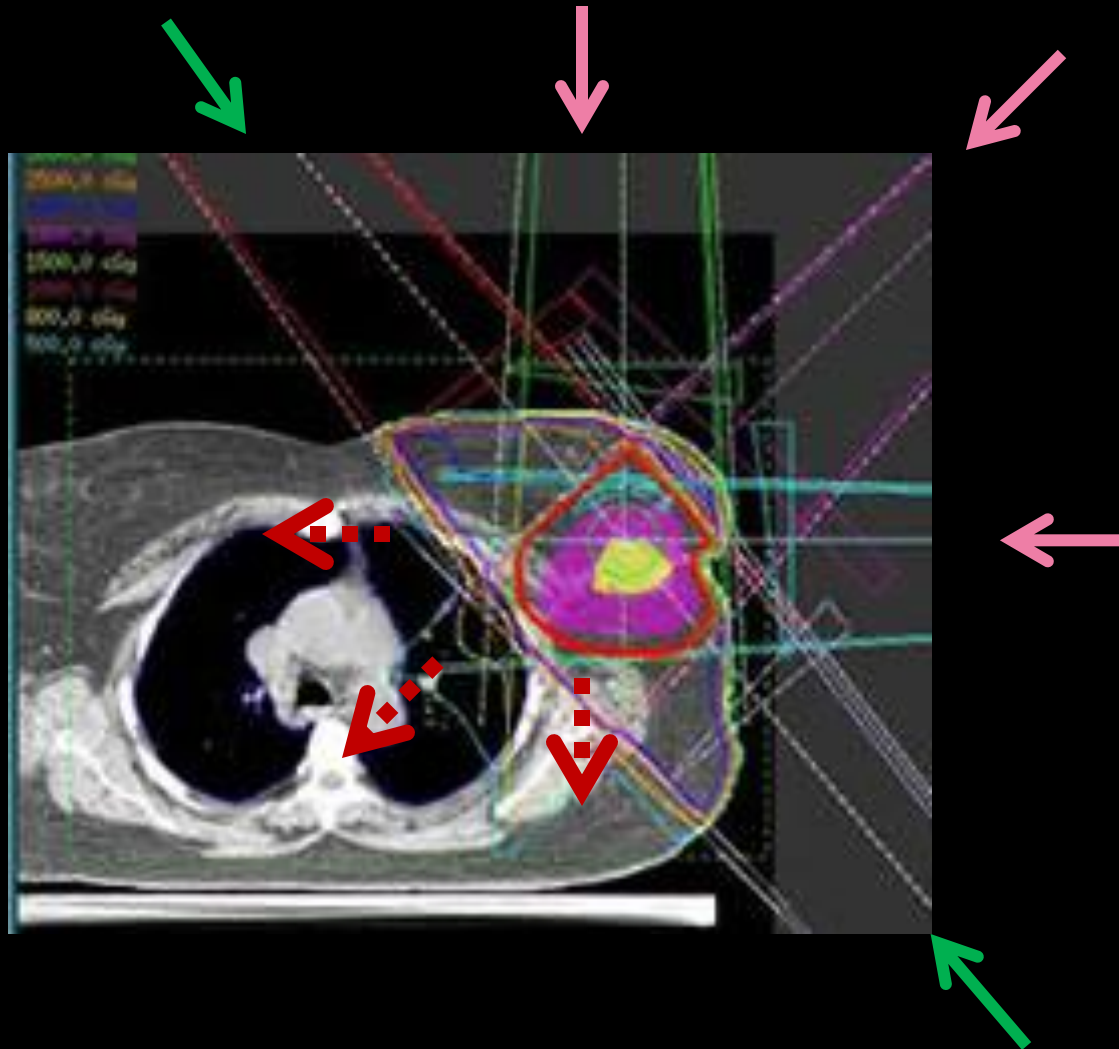


CT Scan Generates a 'Beam's Eye' View of a Tumour Bed Boost Dose



'Advanced' RT Techniques

Exit doses have to go somewhere!

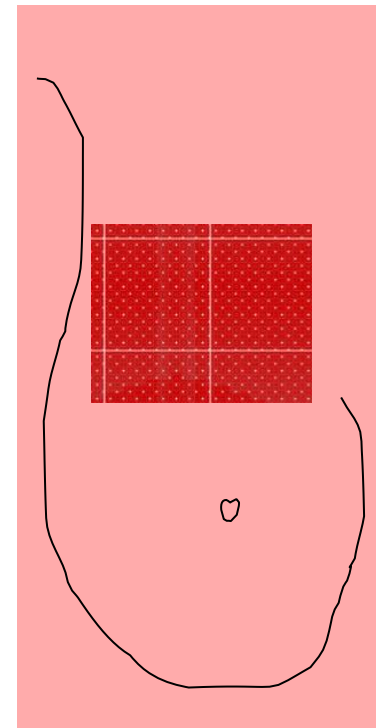
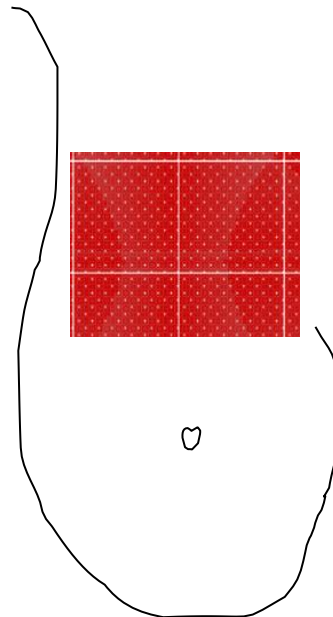
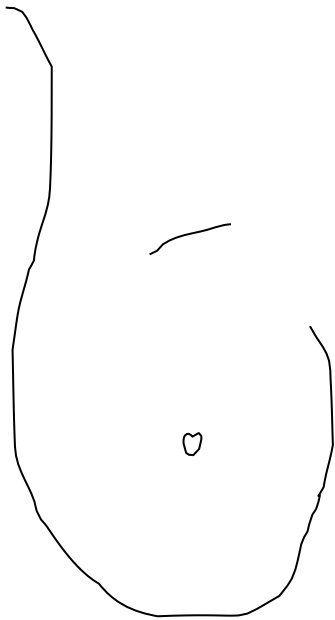


Personalised Radiotherapy: Matching RT to Local Recurrence (LR) Risk

LR Risk: 10-20%
No RT

20%
PBRT

The rest
WBRT



CONCLUSIONS

- Evaluate selective avoidance of RT in low risk subgroups
- Agree subgroups benefitting from IM-SC RT
- Protect the heart
- Partial breast RT may be enough
- Exploit dose intensity gradients
- Beware of 'dose dumping' with advanced RT