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Plan Evaluation in Early Breast Cancers
Hypofractionation Era

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Disclosure: None

COI: None

Information used are from trial protocols available online

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Introduction

I will not discuss about:

- Radiobiological evaluation
- Nodal irradiation
- Brachytherapy plan evaluation

Disclosure: None

COI: None

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Scenarios

1. Whole Breast Radiation
2. Sequential Boost
3. Simultaneous Boost
4. External Beam APBI
5. Brachytherapy Based APBI
6. IORT
7. PBT

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Relevant Trials

- Ontario Clinical Oncology Group (OCOG) Trial
- Royal Marsden GOC trial
- START-A
- START-B
- UK FAST Trial
- IMPORT High
- IMPORT Low
- UK FAST Forward
- HYPORT ART
- NRG Oncology RTOG 1005

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Trial Summaries

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Ontario COG trial

Arm	Dose (Gy)	No of Fractions	Dose/Fx (Gy)	Time (Weeks)
Control Arm	50	25	2	5
Test Arm1	42.5	16	2.66	3

Royal Marsden GOC Trial

Arm	Dose (Gy)	No of Fractions	Dose/Fx (Gy)	Time (weeks)
Control Arm	50	25	2	5
Test Arm1	42.9	13	3.3	5
Test Arm2	39	13	3	5

UK START A

N	Dos(Gy)	No .of Fractions	Dose/Fx (Gy)	Time (Weeks)
749	50	25	2	5
750	41.6	13	3.2	5
737	39	13	3	5

UK START B

N	Dos(Gy)	No .of Fractions	Dose/Fx (Gy)	Time (Weeks)
1105	50	25	2	5
1110	40	15	2.67	3

UK FAST Trial

N	Dose (Gy)	No of fractions	Dose/Fx (Gy)	Time (weeks)
302	50	25	2	5
308	30	5	6	5
305	28.5	5	5.7	5

UK FAST FORWARD

N	Dose (Gy)	No of Fractions	Dose/Fx (Gy)	Time (weeks)
1361	40.05	15	2.67	3
1367	27	5	5.4	1
1368	26	5	5.2	1

IMPORT HIGH

N	Dose (Gy)	No of fractions	Dose/Fx (Gy)	Time (weeks)
656	40 (WB) 16 (Boost)	15 8	2.67 2	5
668	36 (WB) 40 (PB) 48 (TB)	15	2.4 2.67 3.2	5
654	36 (WB) 40 (PB) 52.5 (TB)	15	2.4 2.67 3.5	5

IMPORT LOW

N	Dose (Gy)	No of fractions	Dose/Fx (Gy)	Time (weeks)
674	40 (WB)	15	2.67	5
673	36 (WB) 40 (PB)	15		5
669	40 (PB)	15	5.7	5

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Dose (Gy)	No of fractions	Dose/Fx (Gy)	Time (weeks)
50/42.7 (WB) 12/14 (Boost)	25/16 6/7	2/2.67 2	6.5/4.5
40 (WB) 48 (Cavity)	15	2.67 3.2	3

HYPORT ART

N	Dose (Gy)	No of fractions	Dose/Fx (Gy)	Time (weeks)
1050	40 (WB, CW, SCF) 48 (TB for BCS)	15	2.67 3.2	3
1050	26 (WB, CW, SCF) 32 (TB for BCS)	5	5.2 6.4	1

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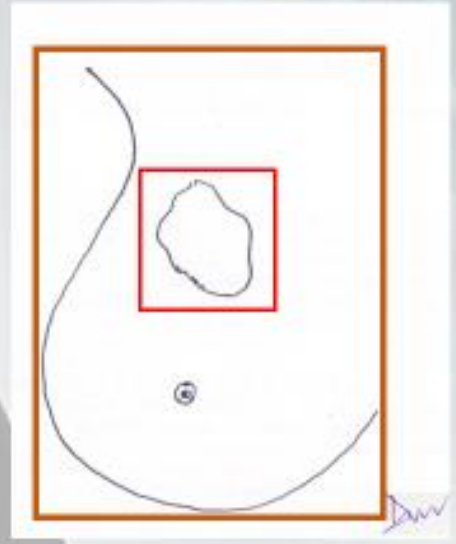
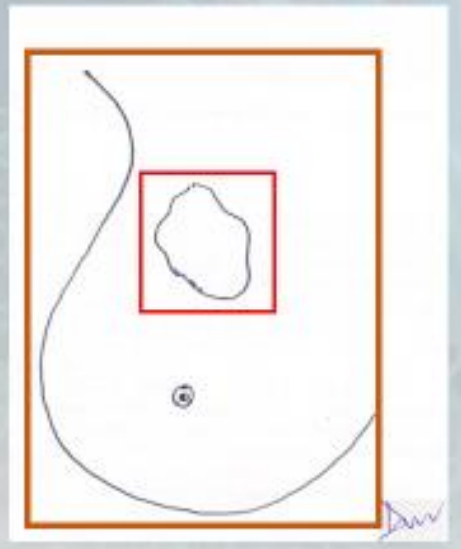
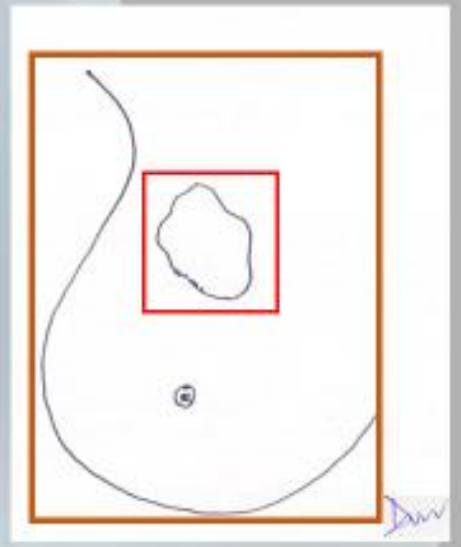
UK FAST FORWARD

CONTROL	TEST1	TEST2
		
40.05Gy/15fx/3week	27 Gy/5 fx/1week	26 Gy/5 fx/1week

- All patients under 40 years
- 40-49 years with grade 3 tumours and/or LVI.
- 50-59 years with adverse prognostic factor, grade or LVI

→ ± Sequential Boost 10Gy/5Fx or 16Gy/8fx

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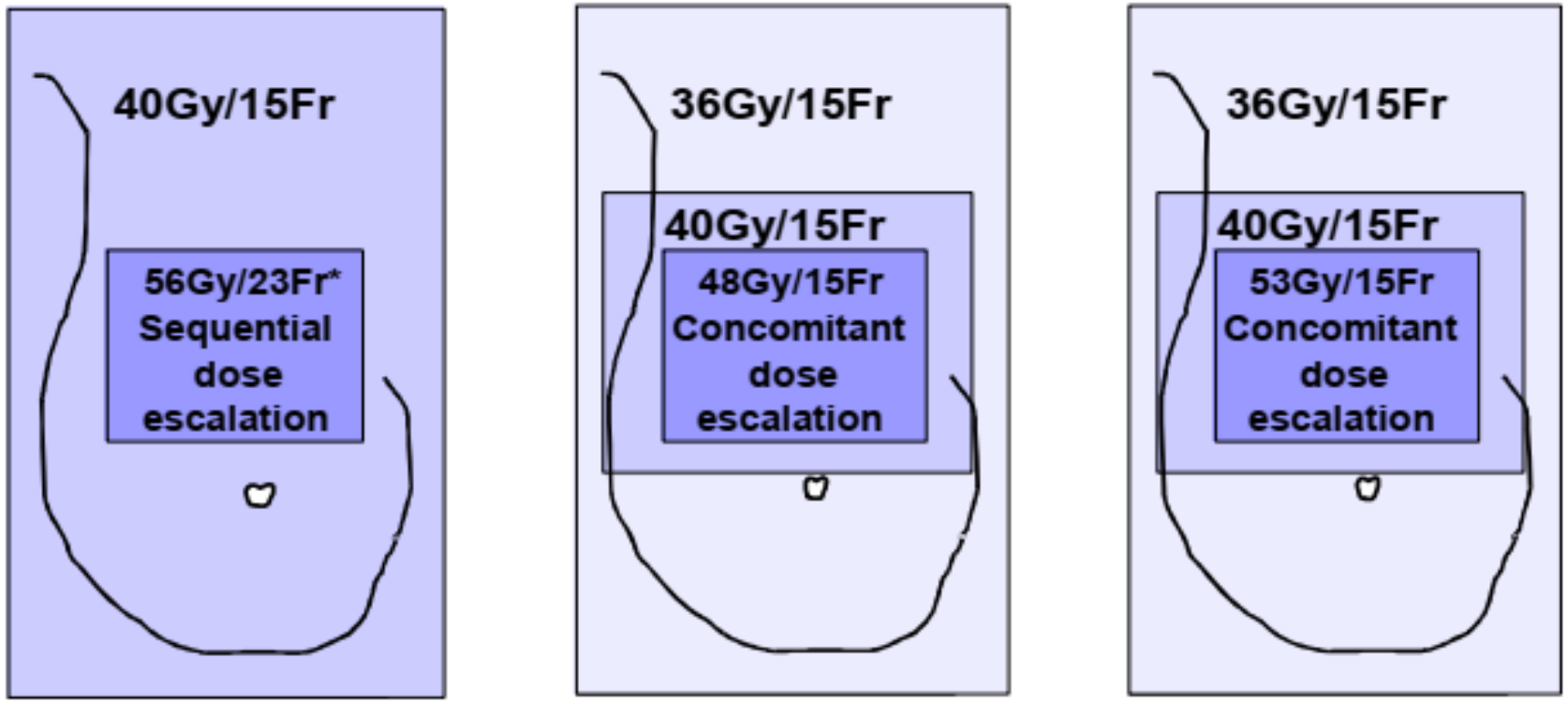

*56 Gy/23F represents 40 Gy/15 F to whole breast plus 16 Gy/8 F sequential photon boost.

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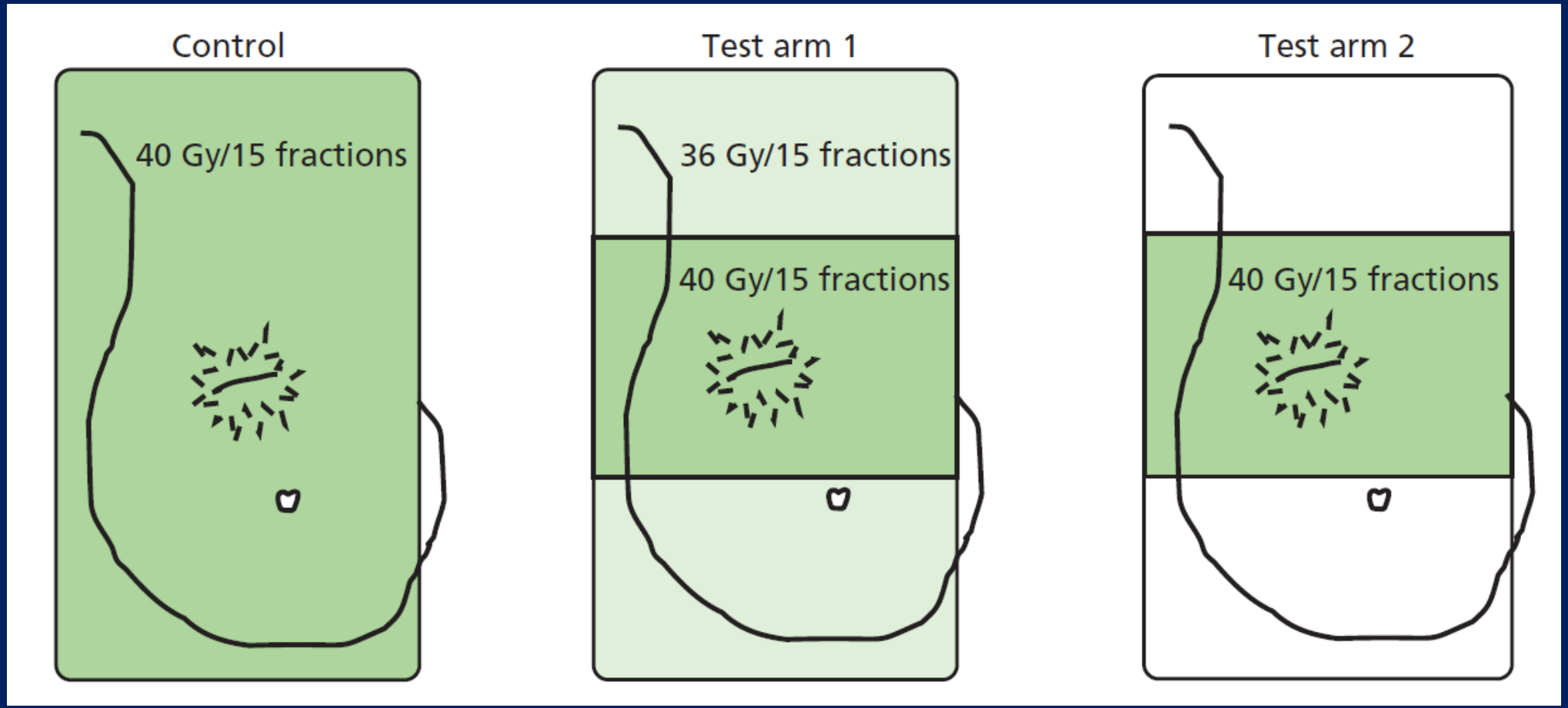

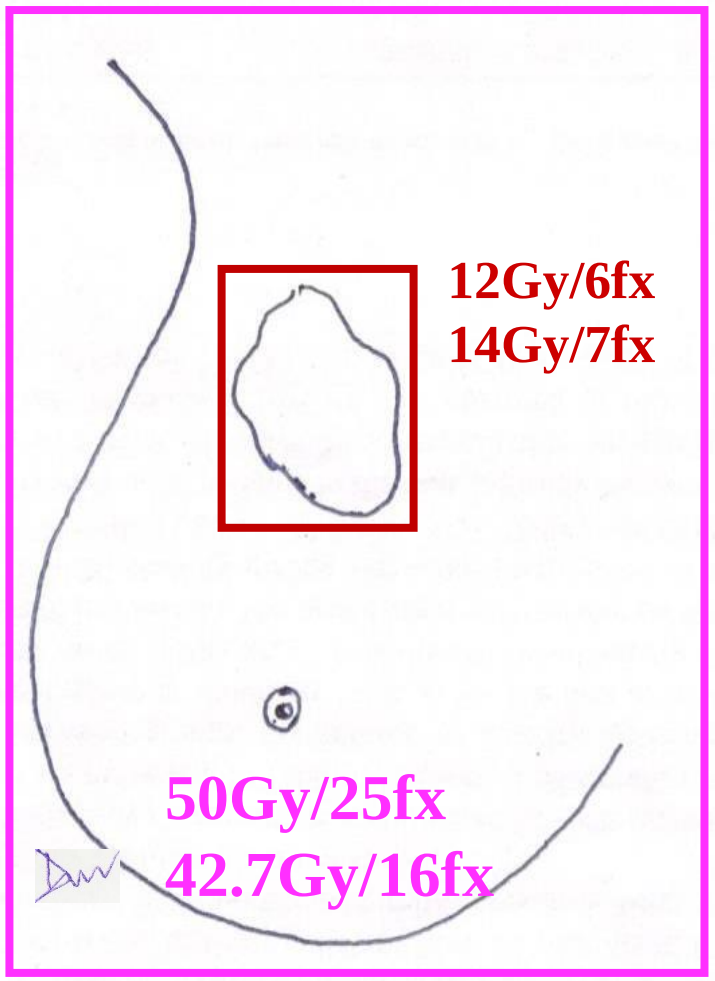

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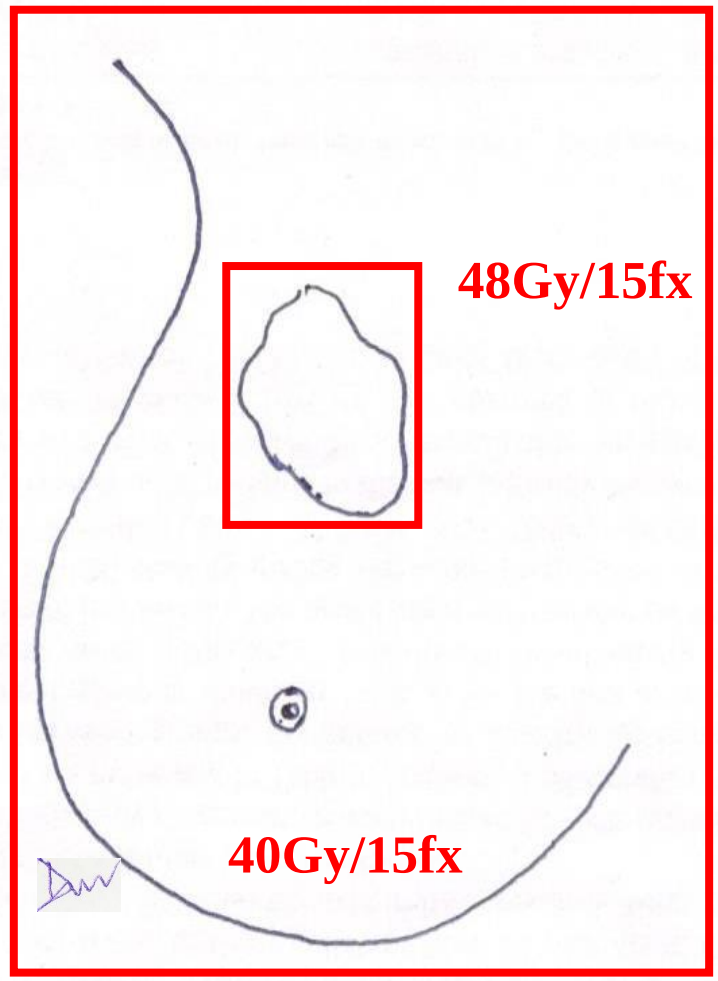

25+6 or 25+7 fraction
Sequential

15 fractions
Concurrent

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Principles of Radiation Treatment

- Maximize target coverage
- Minimize normal organ dose
- Maximize chance of cure
- Minimize chance of toxicity
- Functional preservation
- Cosmetic outcome
- Quality of life

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Principles of Evaluation

Dynamic Process

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Principles of Evaluation

Know the target

Guidelines

Check contouring
Target and OAR

Know critical organs

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Principles of Evaluation

- Dose Constraints
- Standard / Protocol Specific
- Understanding limitation of systems
- Plan acceptance criteria
- Technique dependent

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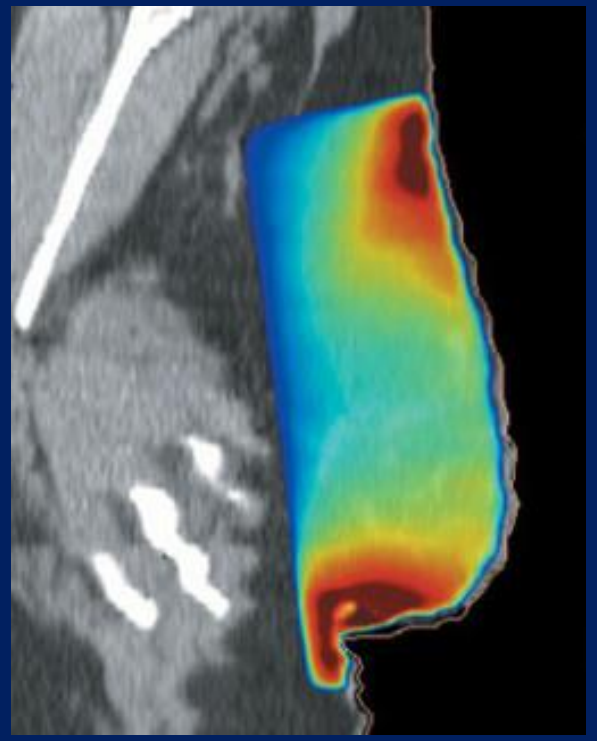
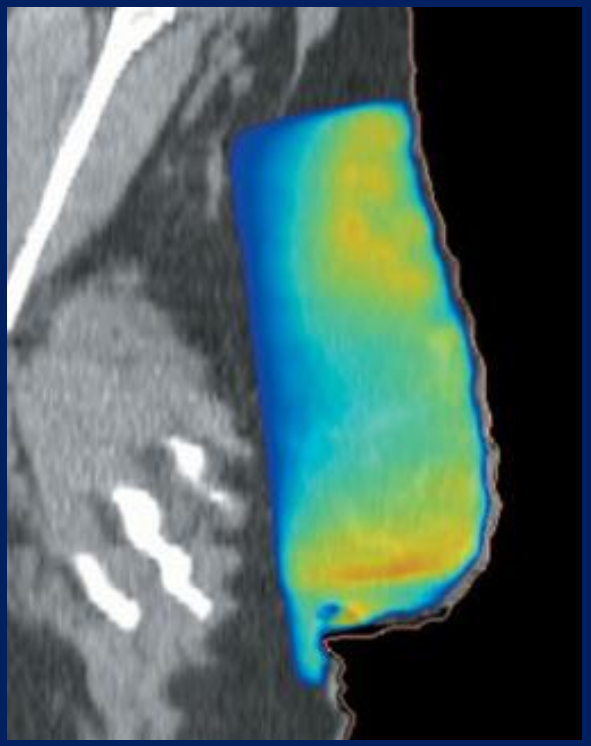
Principles of Evaluation

Qualitative analysis





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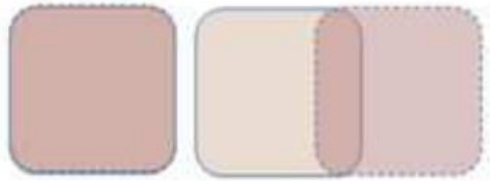
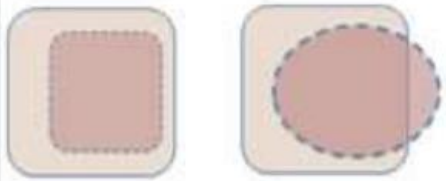
Principles of Evaluation

Quantitative analysis

DVH analysis

Dosimetric indices:

- Prescription isodose to target volume (PITV)
- Conformity index (CI)
- Homogeneity index (HI)
- Target Coverage Index (TCI)
- Modified Dose Homogeneity Index (MHI)
- Conformity Number (CN)
- Quality Factor (QF) for PTV
- Dmax
- Dmean
- Critical Organ Scoring Index (COSI)

Index	Formula	Concept	Value = 1	Value <1 or value >1
PITV (prescription isodose to target volume)	$PITV = \frac{PIV}{TV}$			
CI (conformity index)	$CI = \frac{PTV_{PD}}{PIV}$			
TCI (target coverage index)	$TCI = \frac{PTV_{PD}}{PTV}$			
CN (conformity number)	$CN = TCI \times CI = \frac{PTV_{PD}}{PTV} \times \frac{PTV_{PD}}{PIV}$			

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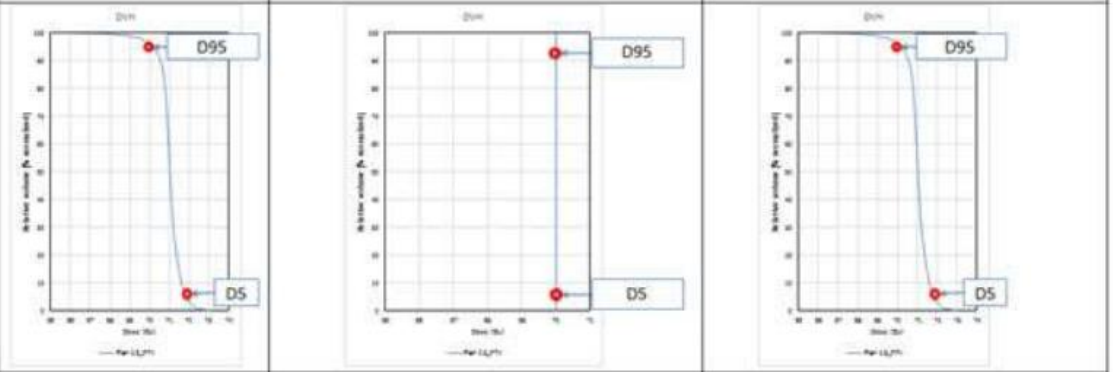
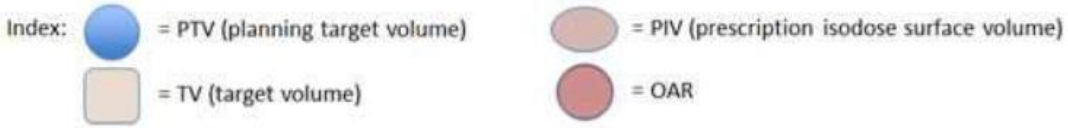
HI (homogeneity index)	$HI = \frac{D_{max}}{PD}$	
MHI (modified homogeneity index)	$MHI = \frac{D_{95}}{D_5}$	
COSI (critical organ scoring index)	$COSI = 1 - \sum_{i}^{n} W_i \frac{V_i(OAR) \geq tol}{TC}$	



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Plan Acceptance Criteria

Protocol Specific

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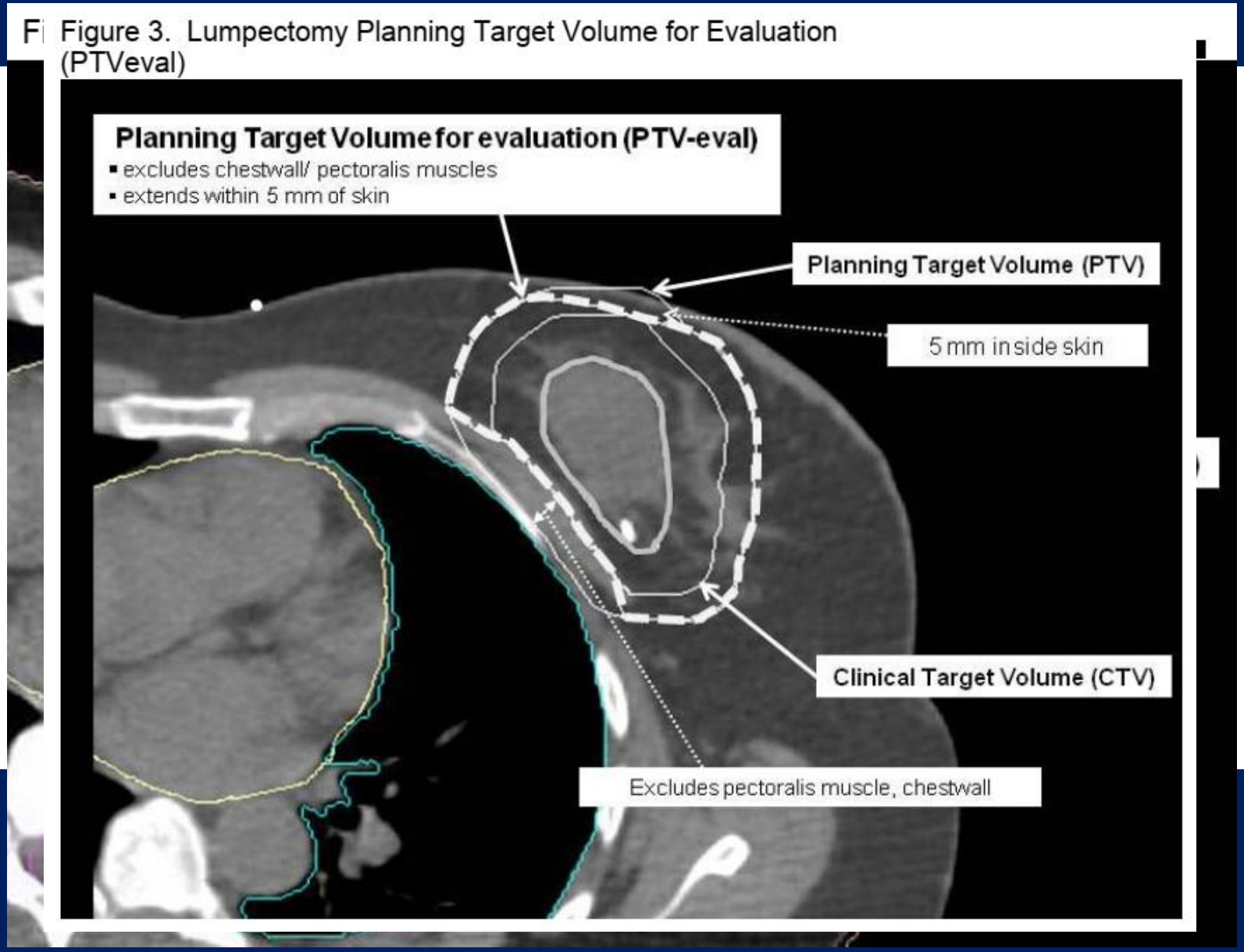
Figure 3. Lumpectomy Planning Target Volume for Evaluation (PTVeval)



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ARM I Standard Whole Breast Irradiation with Sequential boost

Lumpectomy PTV Eval:

- Per Protocol: The maximal point dose will not exceed 71.3-73.6 Gy which is 115% of the boost prescribed dose of 62-64 Gy (or will not exceed 62.9-65.2 Gy which is 115% of 54.7-56.7 Gy if hypofractionated whole breast fractionation is used).
  Variation Acceptable: The maximal dose point is will not exceed 74.4-76.8 Gy which is 120% of the boost prescribed dose of 62-64 Gy (or maximal dose will not exceed 65.6-68 Gy which is 120% of 42.7 if hypofractionation is used).
- Optional constraint: Conformity Index (CI): defined as "the ratio of the volume covered by the 95% prescription isodose over the volume of lumpectomy PTV Eval. Per Protocol: CI is no less than 0.95 and no more than 2.5.
  Variation Acceptable: CL is no less than 0.9 and no more than 3

hypofractionation whole breast fractionation is used).

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Contralateral Breast

- Per Protocol: The maximum dose to contralateral breast does not exceed

Heart

- Per Protocol: No more than 5% of the whole heart exceeds 20 Gy for left-

Thyroid

ARM 1 if prescribed 62-64 Gy:

- Per Protocol: The maximum point dose does not exceed 2% of the prescribed dose (Maximum point dose does not exceed1.24-1.28 Gy).
  Variation Acceptable: The maximum point dose does not exceed 3% of the prescribed dose (Maximum point dose does not exceed 1.86-1.92 Gy).

.

ARM 1 if prescribed 54.7-56.7 Gy:

- Per Protocol: The maximum point dose does not exceed 2% of the prescribed dose (Maximum point dose does not exceed 1.09-1.13 Gy).
  Variation Acceptable: The maximum point dose does not exceed 3% of the prescribed dose (Maximum point dose does not exceed 1.64-1.70 Gy

Every attempt should be made to make the cardiac exposure to radiation as low as possible.

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ARM II Hypofractionated Whole Breast Irradiation with Concomitant Boost

Breast PTV Eval

Heart

- Per Protocol: No more than 5% of the whole heart exceeds 16 Gy for left-sided breast cancers, and 0% of the heart exceeds 16 Gy for right-sided breast cancers.
- Variation Acceptable: No more than 5% of the whole heart exceeds 20 Gy for left-sided breast cancers, and 0% of the heart exceeds 20 Gy for right-sided breast cancers.
- Per Protocol: No more than 30% of the whole heart exceeds 8 Gy for left sided breast cancers and no more than 10% of the heart exceeds 8 Gy for right-sided breast cancers.
  Variation Acceptable: No more than 35% of the whole heart exceeds 8 Gy for left-sided breast cancers and no more than 15% of the heart exceeds 8 Gy for right-sided breast cancers.
- Per Protocol: The mean heart dose does not exceed 320 cGy.
  Variation Acceptable: The mean heart dose does not exceed 400 cGy.

Every attempt should be made to make the cardiac exposure to radiation as low as possible.

Thyroid

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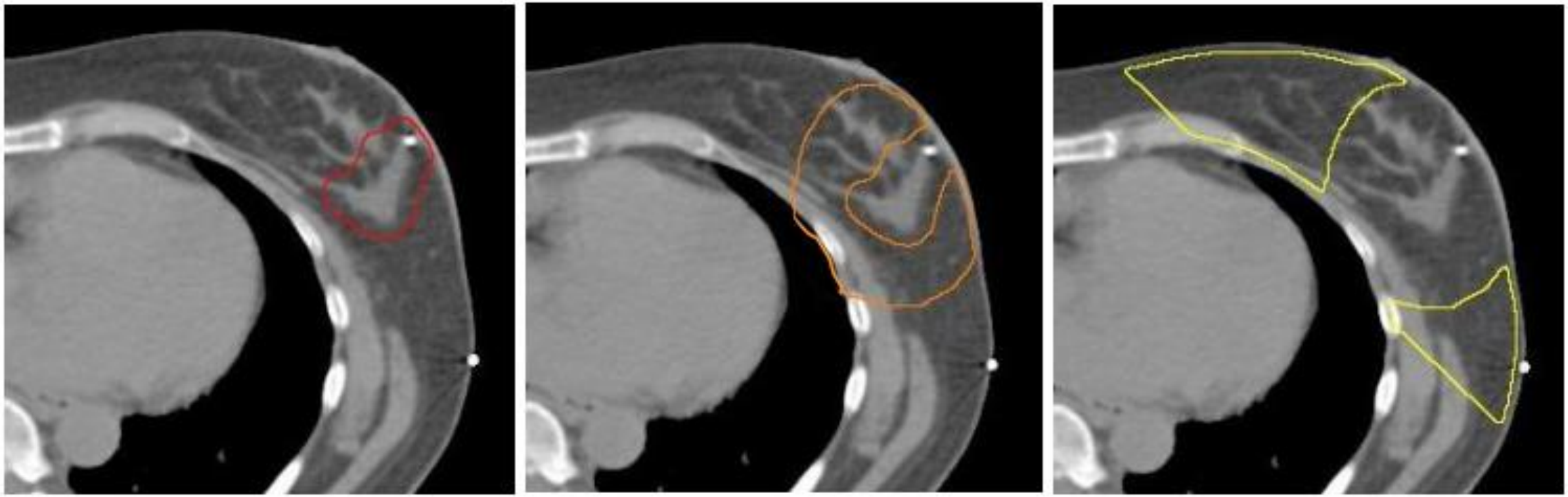
CTV PTV



PTV_{TB} DVH PTV_{PB} - PTV_{TB} PTV_{WB} - PTV_{PB}

Figure 9. Axial slices showing subtracted structures for DVH analysis.

Figure 8. Axial slice showing field-based whole breast PTV

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Control Arm

Volume	Lower dose lim
PTV_{WB} - PTV_{TB}	> 90% of the volu should receive 36
PTV_{TB}	> 95% of the volu should receive 53.2

Organ at risk	Mandatory Constraint	Optimal Constraint
Ipsilateral Lung	V18Gy <15%	V18Gy <10%
		Mean Dose <6Gy
Contralateral Lung	V2.5Gy < 15%	V2.5Gy < 3%
		Mean Dose <1Gy
Heart (Left sided tumour)	V13Gy < 10%	V13Gy < 2%
		Mean Dose < 3Gy
Heart (Right sided tumour)	N/A	V5Gy < 6%
		Mean Dose < 1.7Gy
Contralateral Breast	Mean Dose < 1.5Gy	Mean Dose < 0.5Gy

ence Dose	Upper dose limit
dose = 36 Gy 34 - 37 Gy)	< 5% of the volume should receive > 40 Gy
dose = 40 Gy 40 - 44 Gy)	N/A
dose = 48 Gy 7.5 - 48.5 Gy)	< 3% of the volume should receive > 51.4 Gy with global max < 52.8 Gy

PTV_{TB}	> 95% of the volume should receive 50.4 Gy	median dose = 53 Gy (allow 52.5 - 53.5 Gy)	should receive > 56.7 Gy with global max < 58.3 Gy

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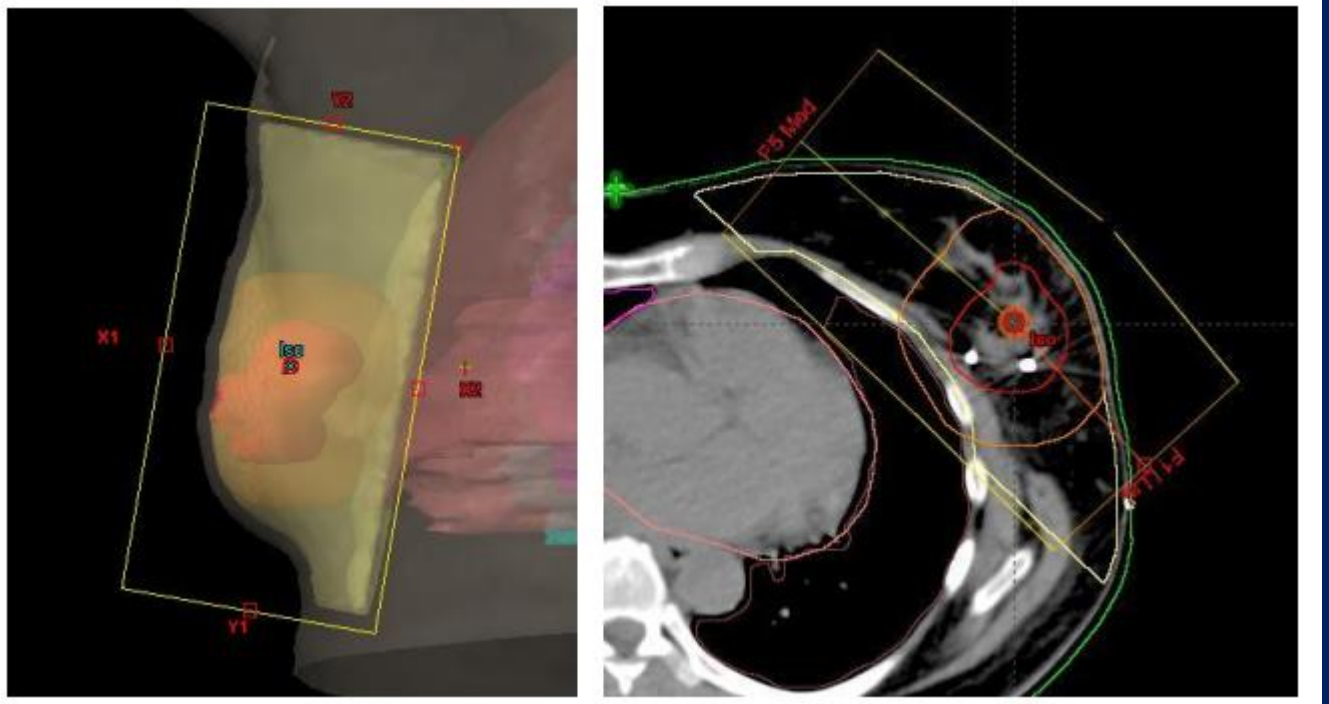

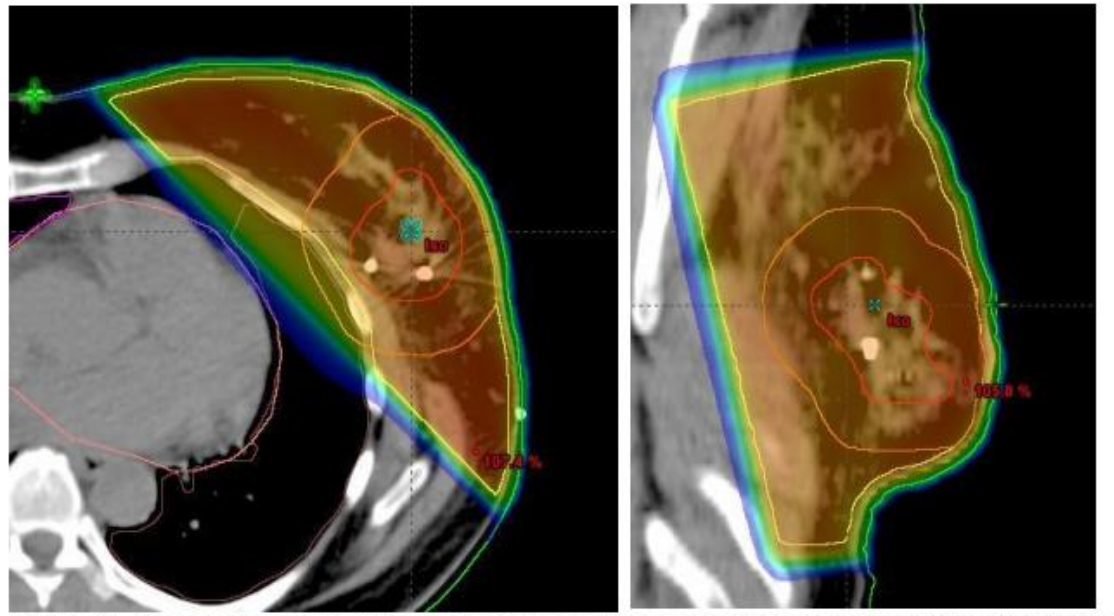

Figure 15. Transverse and sagittal slices with colour wash showing dose distribution from 34Gy base dose plan

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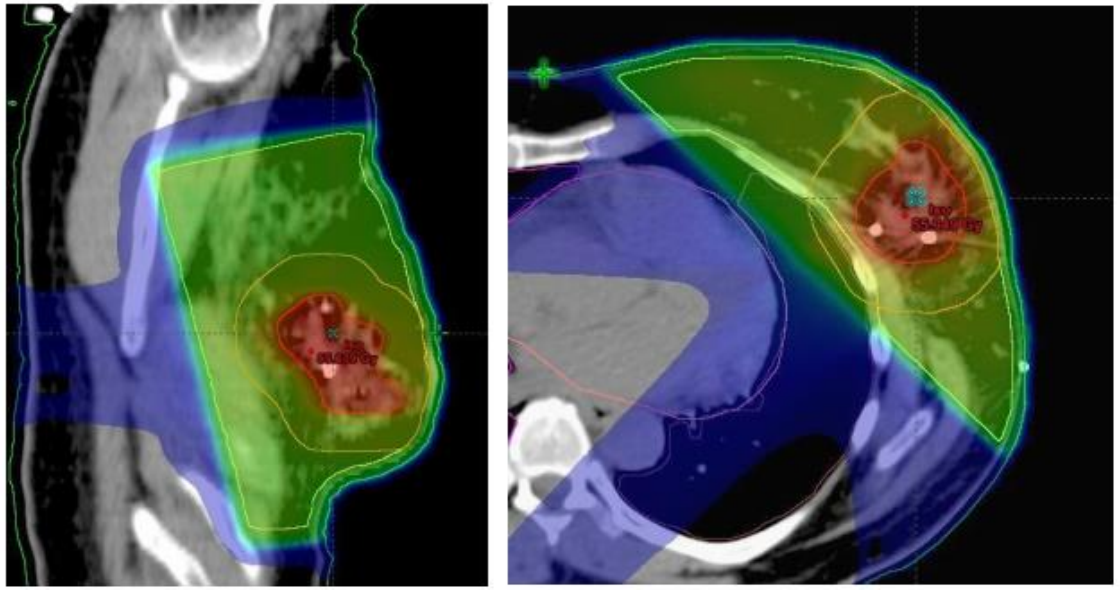

Figure 17. Transverse and sagittal slices showing the combined dose from a base dose plan and boost dose plan for test arm 2 (53Gy total dose)

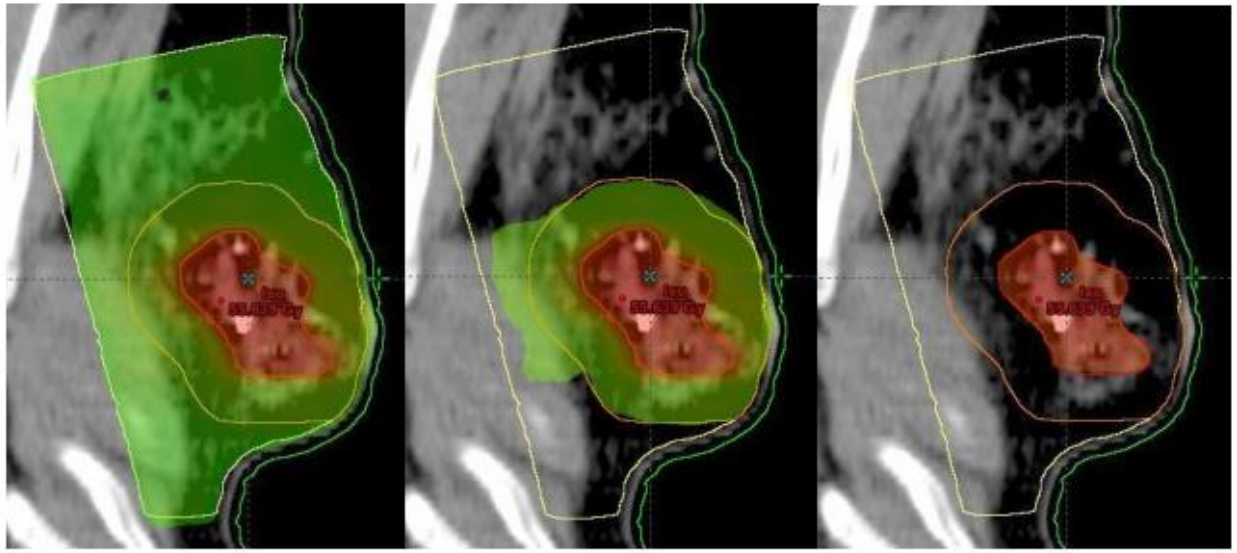

Figure 18. Sagittal slices showing 95% dose coverage for each of the three dose levels in test arm 2 (36Gy, 40Gy and 53Gy).

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UK FAST FORWARD

10.1.1 Whole breast/chest wall, level I-III axilla and/or level IV axilla (SCF)

Trial group	Total dose (Gy)	Dose per fraction (Gy)	Number of fractions	Fractions per week	Treatment time (weeks)
Control Group	40.05	2.67	15	5	3
#Test Group 2	26.0	5.2	5	5	1

Justification for choice of this regimen is found in Appendix 2

UK FAST FORWARD

Lower dose limit	Prescription dose	Upper dose limit
>95% of the volume should receive 95% of the prescribed dose	Use a clinical relevant normalisation point for tangents, seek QA advice for inverse-planned	<5% of the volume should receive ≥105% <2% of the volume should receive ≥107% global max <110% of the prescribed dose

Table 2: Upper and lower dose limits for whole breast/chest wall PTV

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OAR

Dose per fraction (Gy)	Keep 30 % of dose to < 15 % of ipsilateral lung volume	Keep 25 % of dose to < 5 % of heart volume	Keep 5 % of dose to < 30 % of heart volume
2.67	12.0 Gy	10.0 Gy	2.0 Gy
5.2	8.0 Gy	7.0 Gy	1.5 Gy

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Take home messages

1. Plan evaluation is a dynamic process
2. Hypofractionation needs special care
3. Important to know the target, OAR
4. Important to follow trial protocol criteria
5. Heart dose, lung dose and contralateral breast dose
6. Every effort should be made to save heart
7. Skin should be effectively spared for better cosmesis


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