Experience on Hypofractionated Radiotherapy in Post Operative Breast Cancer Patients- in Cancer Center, CMH Dhaka

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Main content

- Rationale
- Clinical evidence & trails
- Result analysis
- Patient outcomes
- Implication in standard practice.

Study overview

- Prospective Observational study
- Single center-Cancer Center, CMH, Dhaka
- IRB registration on 27/05/2018
- Duration: June 2018 to June 2021 (3 years)
- 273 patients of Breast cancer
- Still ongoing till June 2028

Introduction

- Hypofrationated radiotherapy is an evolving treatment approach gaining widesprade acceptance due to clinical benifit & practical advantages.

- Over the past 2 decades numerous clinical trials have evaluated on hypofractionated breast RT.

Objective

Primary end point:

- Locoregional failure
- Acute & late toxicity

Secondary end points

- Locoregional failure free survival (LRFFS)
- Overall survival (OS)

Rationale

Why HFRT?

- Shorter treatment duration .
- More convenient for patients.
- Equivalent local control & survival rates compare to conventional RT
- Reduced healthcare burden and cost.
- Radiobiological advantage is low **α/β** ratio (~4 Gy).

Clinical Trials

ROJ Radiation Oncology Journal

Review Article

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Journey to hypofractionation in radiotherapy for breast cancer: critical reviews for recent updates

Table 1. Patient and treatment characteristics of randomized clinical trials

	START pilot	START A	START B	OCOG	Beijing	Chinese	MDACC	DBCG Hypo	TROG 07.01	FAST	FAST-Forward
Year	1986–1998	1998–2002	1999–2001	1993–1996	2008–2016	2010–2015	2011–2014	2009–2014	2007–2014	2004–2007	2011–2014
n	1,410	2,236	2,215	1,234	820	734	287	1,854	1,608	915	4,096
Standard arm[a]	50 Gy/25 fx	50 Gy/25 fx	50 Gy/25 fx	50 Gy/25 fx	50 Gy/25 fx	50 Gy/25 fx	50 Gy/25 fx	50 Gy/25 fx	50 Gy/25 fx	50 Gy/25 fx	40 Gy/15 fx (3)
Test arm[a]	42.9 Gy/13 fx (5)	41.6 Gy/13 fx (5)	40 Gy/15 fx (3)	42.5 Gy/16 fx (3)	43.5 Gy/15 fx (3)	43.5 Gy/15 fx (3)	42.5 Gy/16 fx (3)	40 Gy/15 fx (3)	42.5 Gy/16 fx (3)	30 Gy/5 fx (5)	27 Gy/5 fx (1)
	39 Gy/13 fx (5)	39 Gy/13 fx (5)								28.5 Gy/5 fx (5)	26 Gy/5 fx (1)
Median age (yr)	55	57	57	NR	49	46	NR	59	58	63	61
< 50 yr (%)	30	23	21	25	48	65	11	11	16	0	15
pT1–2 (%)	94	100	100	100	NR (median 2.5 cm)	100	100	100	> 2.0 cm, 33%	100	98
pN+ (%)	33	29	23	0	100	20	4	0 (macro)	0	0	18
Grade 3 (%)	NR	28	23	19	28	25	24	16	73	11	28
BCS (%)	100	85	92	100	0	100	100	100	100	100	94
Chemotherapy (%)	14	36	22	11	100	65	30	31	0	0	25
RNI (%)	21	14	7	0	100	4	0	0	0	0	0
Boost (%)	75	61	43	0	N/A	99.7	100	23	50	0	25

START, Standardization of Breast Radiotherapy Trial; OCOG, Ontario Clinical Oncology Group; MDACC, MD Anderson Cancer Center; DBCG, Danish Breast Cancer Group; TROG, Trans-Tasman Radiation Oncology Group; BCS, breast-conserving surgery; RNI, regional nodal irradiation.
[a]Total dose/number of fractions (weeks).

Table Clinical and toxicity outcomes of randomized clinical trials

	START pilot (50 Gy vs. 42.9 Gy vs. 39 Gy)	START A (50 Gy vs. 41.6 Gy vs. 39 Gy)	START B (50 Gy vs 40 Gy)	OCOG (50 Gy vs 42.5 Gy)	Beijing (50 Gy vs. 43.5 Gy)	Chinese (50 Gy vs. 43.5 Gy)	MDACC (50 Gy vs. 42.5 Gy)	DBCG Hypo (50 Gy vs. 40 Gy)	TROG 07.01 (50 Gy vs. 42.5 Gy)	FAST (50 Gy vs. 30 Gy vs. 28.5 Gy)	FAST-Forward (40 Gy vs. 27 Gy vs. 26 Gy)
Follow-up (yr)	9.7	9.3	9.9	12	4.9	6.1	4.1	7.3	6.6	9.9	6.0
5-yr IBTR											
Standard	7.9	3.4	3.3	3.2	8.1 (LRR)	1.2	98 (LRFS)		5.1	0.7	2.1
Test	7.1	3.1	2	2.8	8.3 (LRR)	2	99 (LRFS)		5.1	1.0	1.7
	9.1	4.4								0.4	1.4
10-yr IBTR											
Standard	12.1	6.7	5.2	6.7				3.3 (9-yr LRR)		0.7	
Test	9.6	5.6	3.8	6.2				3.0 (9-yr LRR)		1.4	
	14.8	8.1								1.7	
Toxicity											
Excellent or good cosmesis	5-yr: 44% vs. 38% vs. 55%; 10-yr: 29% vs. 26% vs. 42%			5-yr: 79.2% vs. 77.9%; 10-yr: 71.3% vs. 69.8%		3-yr: 89% vs. 89%	3-yr: 73% vs. 78%	5-yr: 75% vs. 80%		18% vs. 24% vs. 18% (mild/marked change)	10% vs. 15% vs. 12% (moderate/marked change)

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diotherapy Trial; OCOG, Ontario Clinical Oncology Group; DBCG, Danish Breast Cancer Group; MDACC, MD Anderson Cancer Center; TROG, Trans-Tasman Radiation Oncology Group.

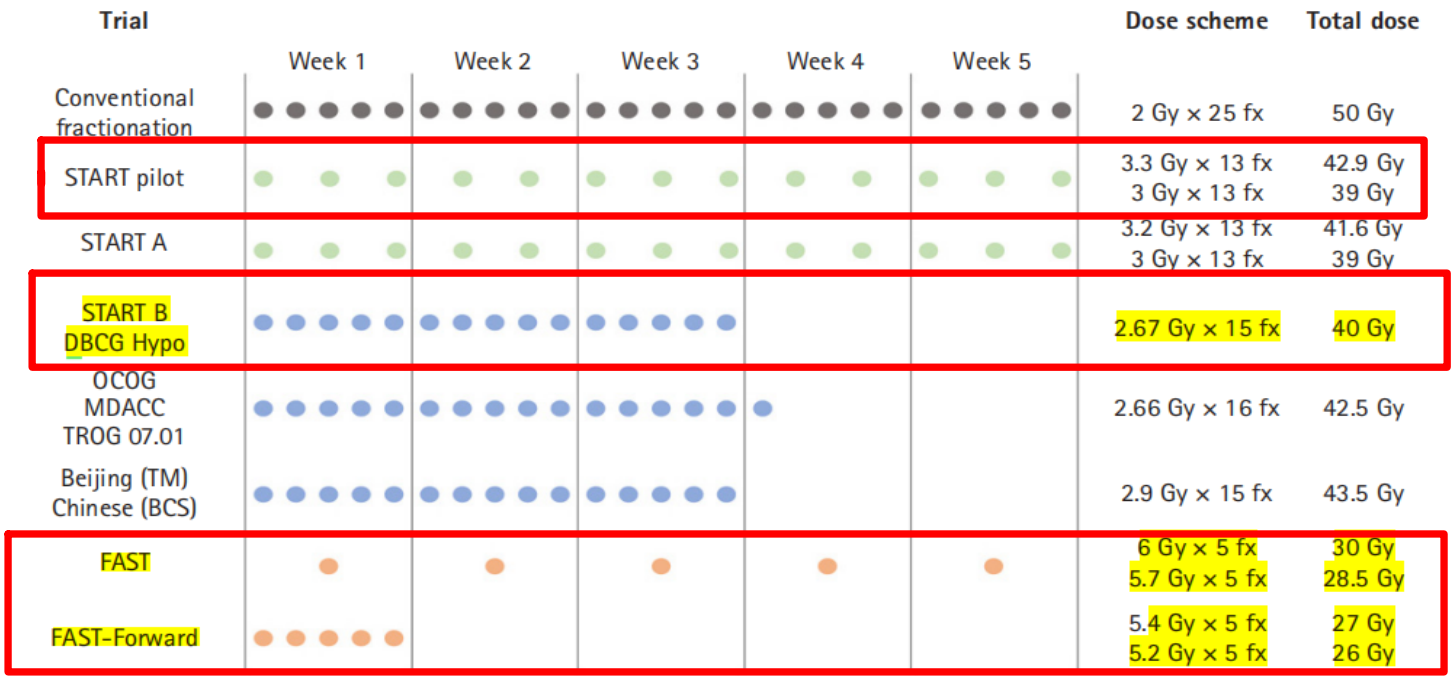

Fig. 2. Treatment schedules and dose regimens of trials for hypofractionated radiation therapy. BCS, breast-conserving surgery; TM, total mastectomy; START, Standardization of Breast Radiotherapy Trial; OCOG, Ontario Clinical Oncology Group; DBCG, Danish Breast Cancer Group; MDACC, MD Anderson Cancer Center; TROG, Trans-Tasman Radiation Oncology Group.

Table 2. Clinical and toxicity outcomes of randomized clinical trials

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Standard	7.9	3.4	3.3	3.2	8.1 (LRR)	1.2	98 (LRFS)		5.1	0.7	2.1
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	14.8	8.1								1.7	
Toxicity											
Excellent or good cosmesis	5-yr: 44% vs. 38% vs. 55%;			5-yr: 79.2% vs. 77.9%;		3-yr: 89% vs. 89%	3-yr: 73% vs. 78%	5-yr: 75% vs. 80%		18% vs. 24% vs. 18% (mild/ marked change)	10% vs. 15% vs. 12% (moderate/ marked change)
	10-yr: 29% vs. 26% vs. 42%			10-yr: 71.3% vs. 69.8%							

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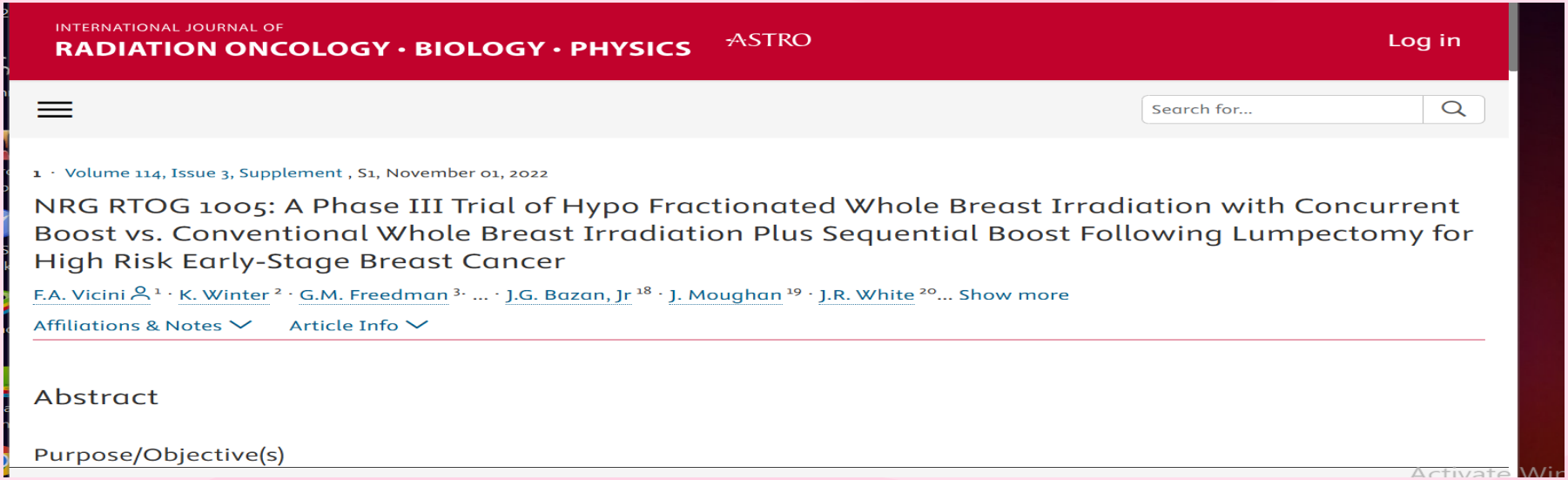
Nalee Kim, et al.

RTOG 1005



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1 · Volume 114, Issue 3, Supplement , S1, November 01, 2022

NRG RTOG 1005: A Phase III Trial of Hypo Fractionated Whole Breast Irradiation with Concurrent Boost vs. Conventional Whole Breast Irradiation Plus Sequential Boost Following Lumpectomy for High Risk Early-Stage Breast Cancer

F.A. Vicini [1] · K. Winter [2] · G.M. Freedman [3] · ... · J.G. Bazan, Jr [18] · J. Moughan [19] · J.R. White [20] ... Show more

Affiliations & Notes Article Info

Abstract

Purpose/Objective(s)

- 40.05 Gy in 15 fractions with SIB to 48 Gy.

cont.

ASTRO Consensus Guidelines:

ASTRO has endorsed HypoRT in WBI regardless of-

- age
- stage
- administration of chemotherapy

ESTRO Guideline:

- HypoRT can be adopted for patients treated with whole breast, chest wall (regardless of reconstruction).

Inclusion Criteria

- ≥ 35 years
- Invasive breast cancer
- pT1-pT3
- pN0-pN1, M0

Exclusion criteria

- ≥ 75 years
- pT4
- pN2-3
- Metastatic & Recurrent cases.

Method

Method

- **Pre Simulation Patient review & assessment**

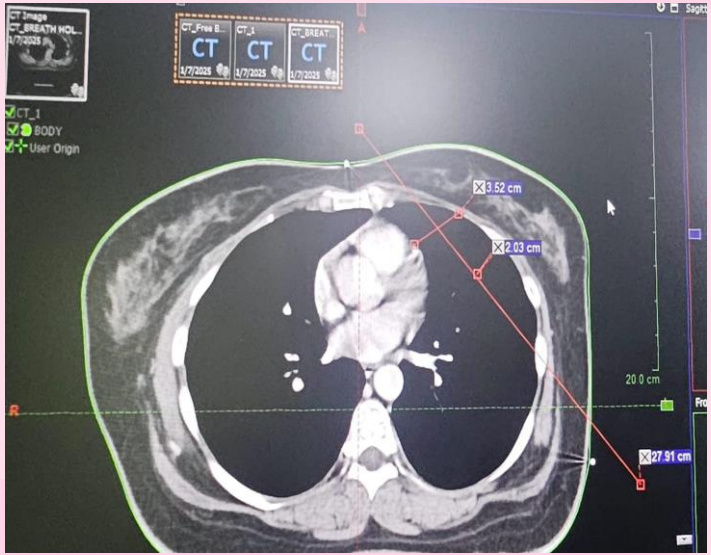
- **CT Simulation:**

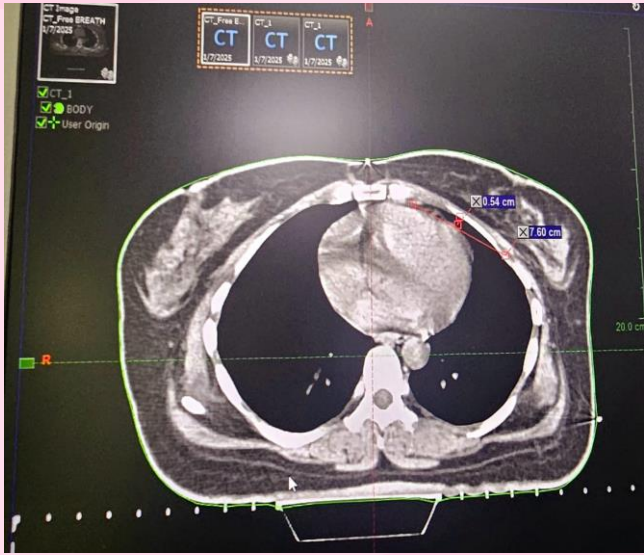
  - Position: supine with arms above the head
  - Immobilization with breast board
  - CT scanning from CC to L2/3 vertebrae
  - Slice thickness 3 to 5 mm
  - All surgical scars marked with wire.

Method cont.

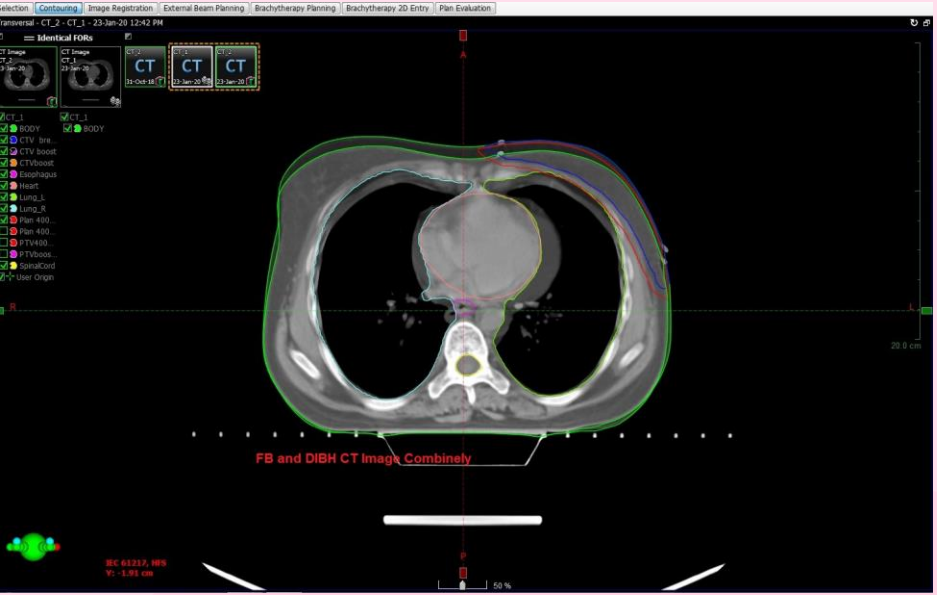
- **Target volume delineation** :

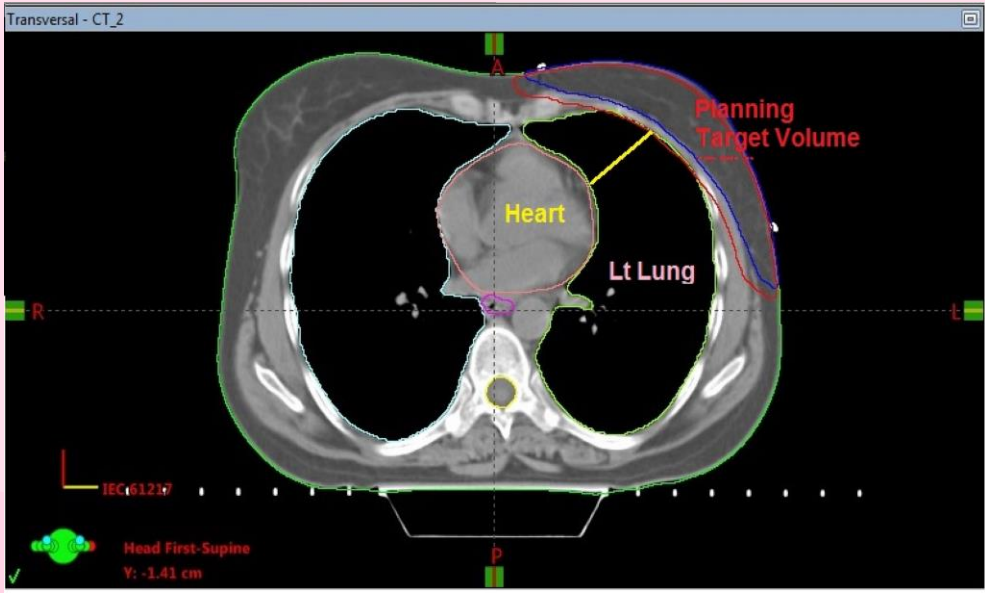
As per Breast cancer RTOG & ESTRO consensus guideline.





Target volume delineation





Method cont.

- **Dose prescription:**
  - 40.05 Gy in 2.67 Gy/fx in 15 fxs (over 3 weeks) **mostly used**
  - 42.5 Gy in 2.66 Gy/fx in 16 fxs (over 3.2 weeks)
  - 10Gy in 4-5 fxs for Boost.

- **Radiation technique:**
  - 3DCRT and IMRT by LINAC
  - 6 MV photon

IMRT plan


IMRT 4005/15 - Treatment Approved - Transversal - CT_Sharmin
Color wash [cGy]
4441.9
4441.9
3804.7
3804.7
R
L
P
Y: -2.50 cm
3D
DVH
BEV
Arc
IMRT 4005/15 - Treatment Approved - Model View - CT_Sharmin
3D Dose MAX: 4441.9 cGy
3D MAX for Plan_4005/15: 4438.4 cGy
3D MIN for Plan_4005/15: 2360.5 cGy
3D MEAN for Plan_4005/15: 4206.6 cGy
IEC 61217
Head First-Supine
IMRT 4005/15 - Treatment Approved - Frontal - CT_Sharmin
H
F
Z: 8.01 cm
IMRT 4005/15 - Treatment Approved - Sagittal - CT_Sharmin
X: 9.24 cm

Plan evaluation

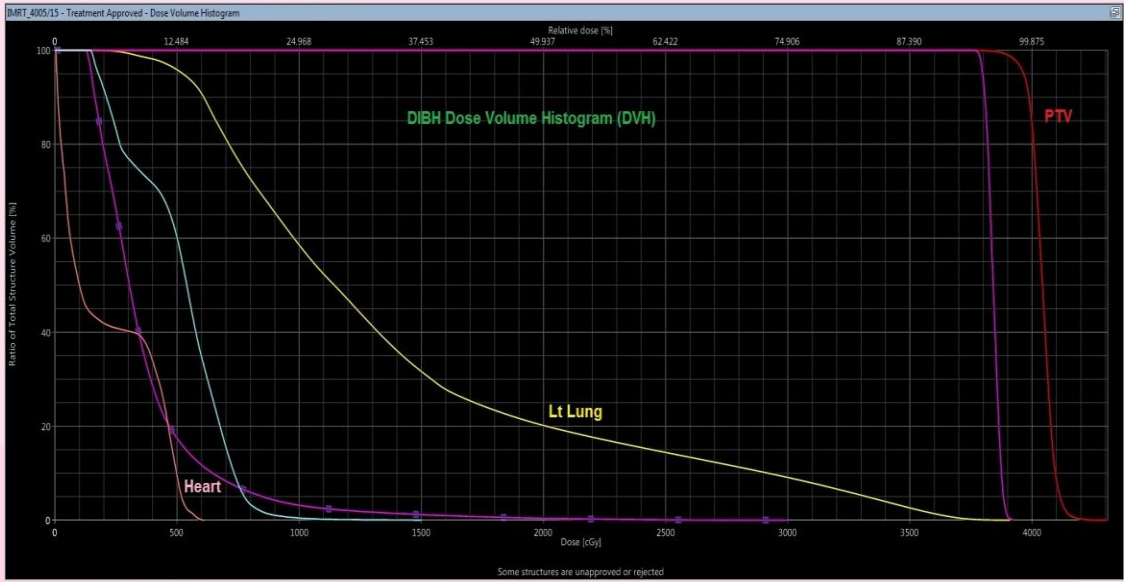
- **Target coverage and dose distribution:**

CTV Coverage:

- 95% CTV ≥ 95%
- Dmax preferably ≤ 107 % of prescribed dose.

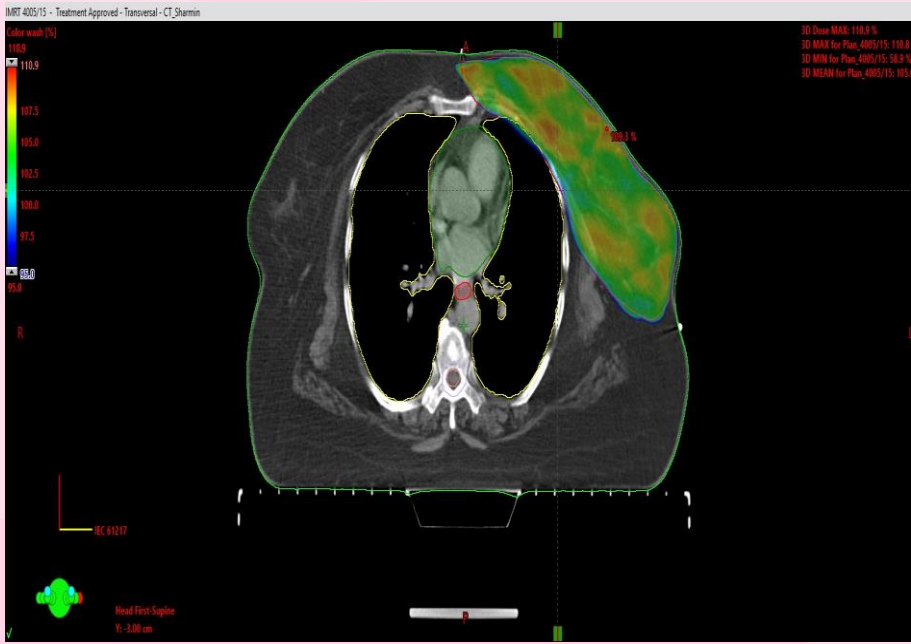
PTV coverage:

- V95 PTV ≥ 95%



Plan evaluation cont.

- **Dose distribution and isodose review**: Check for-
  - Hotspot (>107%) in Normal tissue
  - Cold spot (<95%) in PTV
  - Dose fall of outside PTV
- **Beam arrangement & Plan Quality Checks**
- **Final plan approval**



Plan evaluation cont.

❑ **OAR Dose constraint:**

- Lung (Ipsilateral)

V20 ≤ 20 to 25%
V10 ≤ 40%
Mean Lung dose ≤ 7Gy

- Lung (Contralateral)

Mean dose ≤ 3Gy
V5 ≤ 10%

- Contralateral Breast < 3 Gy

- Heart (MHD):

≤ 4Gy (preferably <3 Gy)
V25 ≤ 10 %
V30 ≤ 5%

- Brachial plexus (if S/C included) 47 Gy Dmax

- Oesophagus Mean < 11 Gy

- Spinal Cord 30 Gy Dmax

Plan evaluation cont.

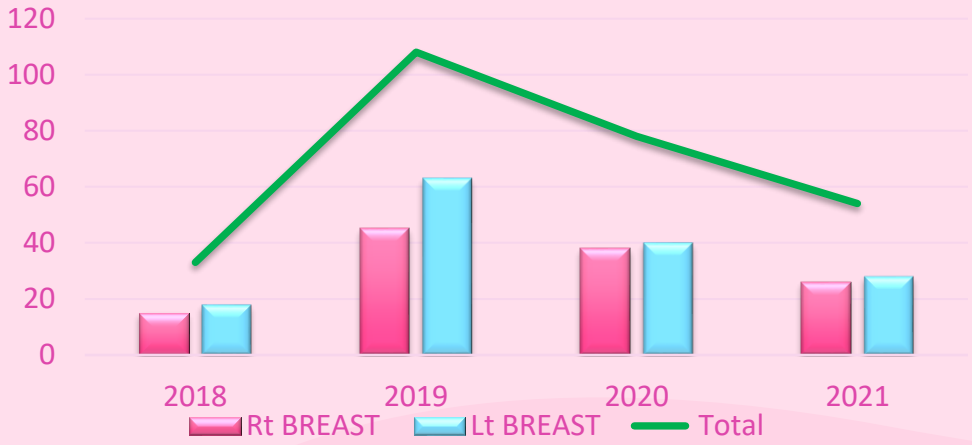
- Patient specific QA
- Patient set up verification by Daily KV-KV image verification.
- Treatment delivery

Patient assessment

- Weekly OPD review:
  - Acute skin toxicity
  - Routine investigations
  - Management as per patient’s complaints.

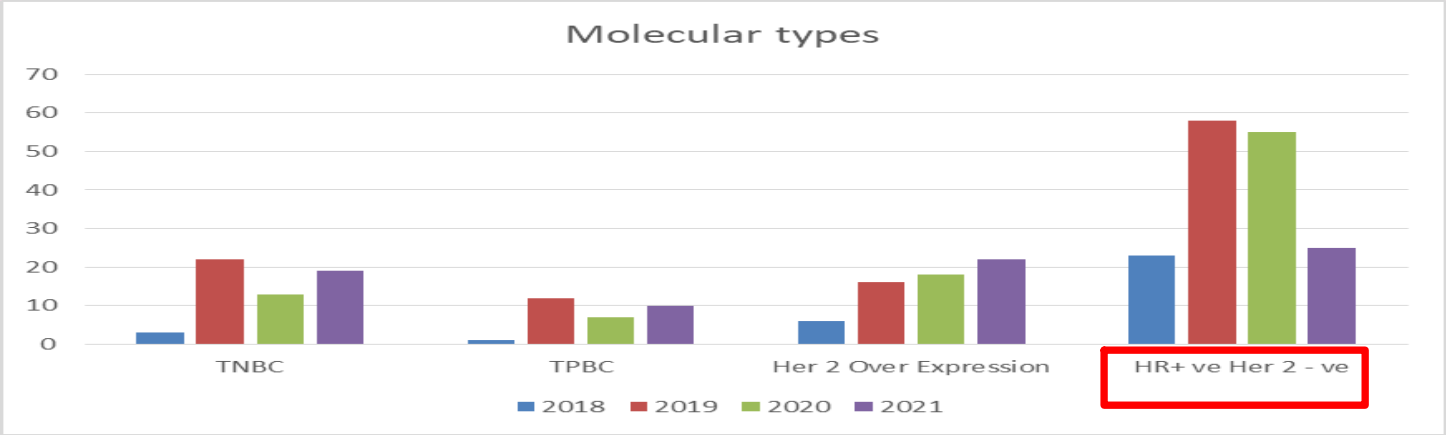
Result

Result - Rt/Lt Breast:



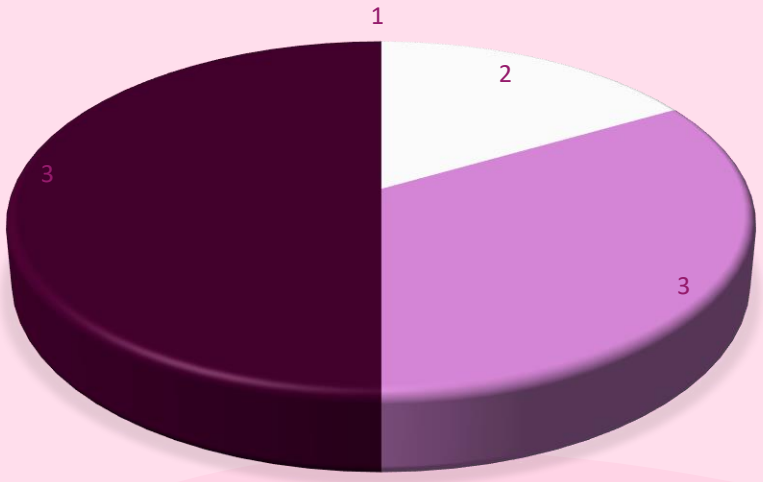
YEAR	Rt BREAST	Lt BREAST	Total
2018	15	18	33
2019	45	63	108
2020	38	40	78
2021	26	28	54
2022	30	28	58
2023	73	58	131
2024	43	55	98
2025	10	10	20
	280	300	580

Result - Molecular types:



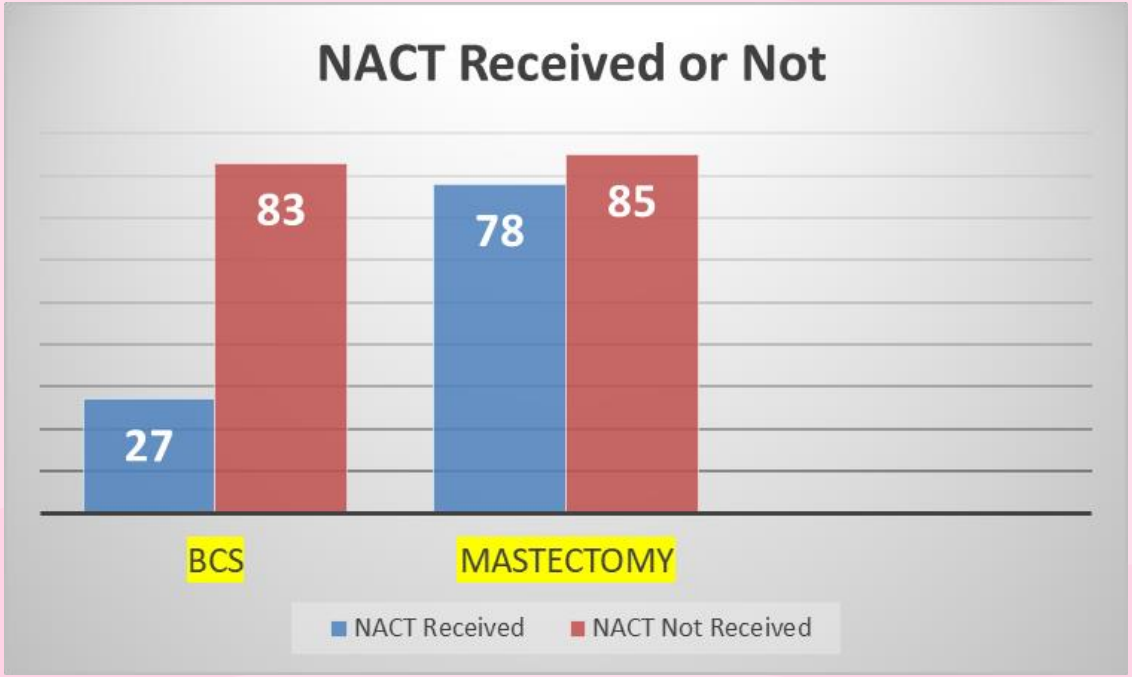
Year	TNBC	TPBC	Her 2 Over Expres	HR+ ve Her 2 - ve
2018	3	1	6	23
2019	22	12	16	58
2020	13	7	18	55
2021	19	10	22	25

Result - Tumor Grade:

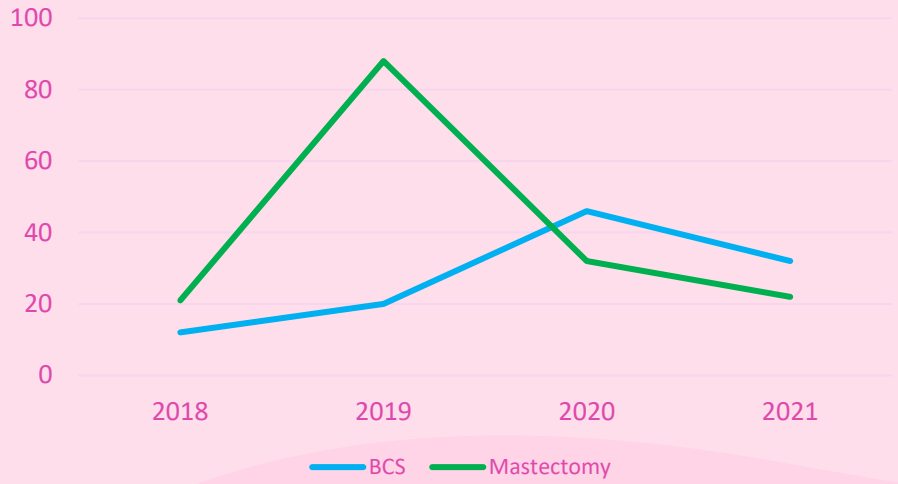


Tumor Grade	
1	114
2	81
3	68

Result - NACT:

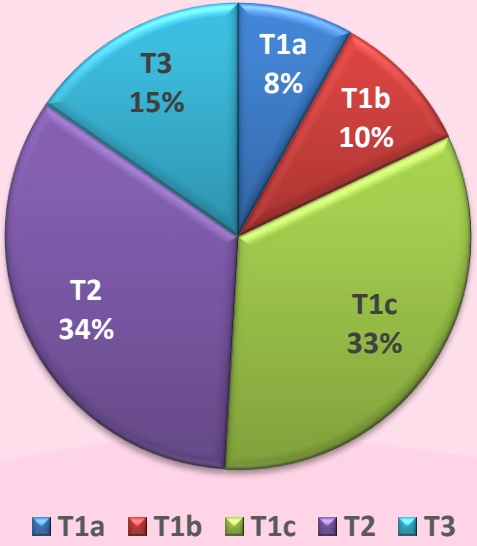

NACT Received or Not
83
78
85
27
BCS
MASTECTOMY
NACT Received
NACT Not Received

Result - Surgery:



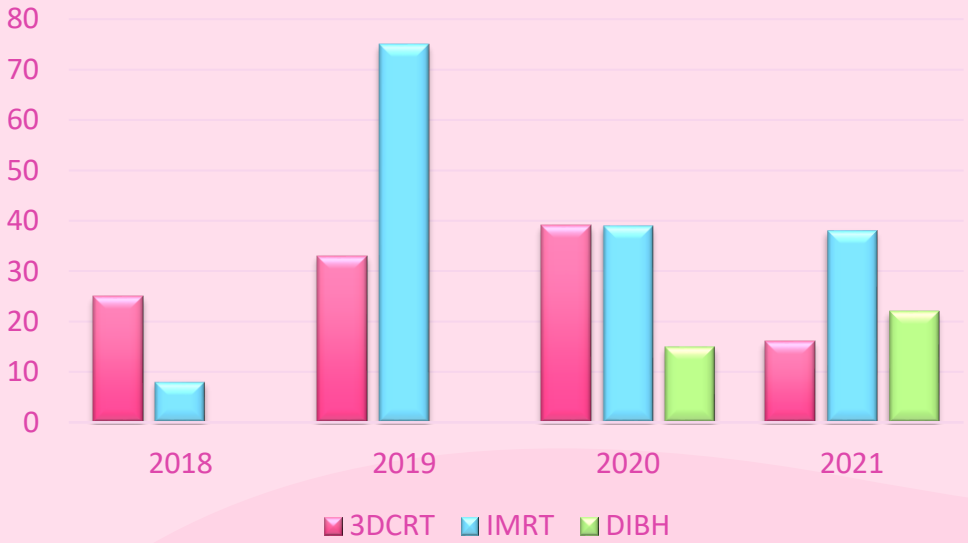
YEAR	BCS	Mastectomy
2018	12	21
2019	20	88
2020	46	32
2021	32	22
TOTAL	110	163

Result - pT stage:



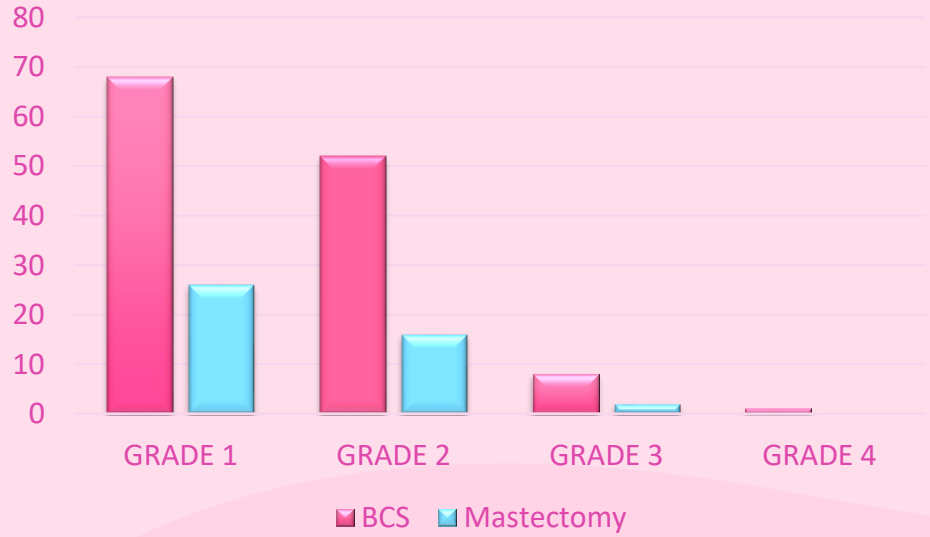
Pathological T-stage	
T1a	22
T1b	27
T1c	90
T2	92
T3	42

Result - IMRT/3DCRT:



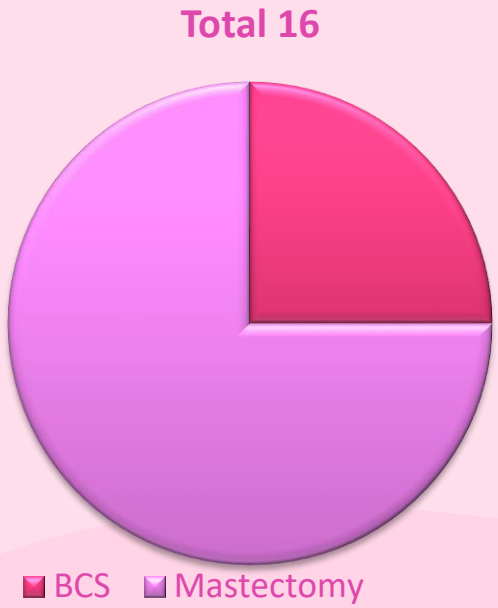
YEAR	3DCRT	IMRT	DIBH
2018	25	8	0
2019	33	75	0
2020	39	39	15
2021	16	38	22
2022	11	45	19
2023	13	118	22
2024	14	84	32
2025	5	15	5
	156	422	115

Result - Skin Toxicity:



TOXICTY	BCS	Mastectomy
GRADE 1	68	26
GRADE 2	52	16
GRADE 3	8	2
GRADE 4	1	0

Result - Lymphedema:



Lymphedema	BCS	Mastectomy
Total 16	4	12

Interpretations

- Skin toxicity
  - Grade II > BCS
  - Grade I > BCS

- Lymphedema
- Dysphagia
- Shoulder stifness

Limitations

- Single center based study.
- No subgroup analysis.
- Irregular FU of Patients.

Take home massage

To achieve radiobiological advantage of HFRT-

- Comprehensive training.
- Motion management system RGS / DIBH
- Cardiac sparing
- Stringent quality assurance
- Daily image guidance.

References

- START Trials (UK).
- Canadian Hypofractionation Trial.
- FAST-Forward Trial.
- RTOG 1005 Trial.
- ASTRO 2018 Consensus Guidelines.
- NCCN Guidelines.
- Int J Radiat Oncol Biol Phys. 2023

Thank You