

29-31 January 2025 Olympic hotel,Tehran ,IRAN

Title: Latest Techniques in Breast Cancer Radiotherapy "Developments from 2024"

Content: Overview of the presentation's focus on recent advancements in radiotherapy for breast cancer treatment

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Introduction

- Breast cancer is most prevalent cancer in world
- Breast cancer incidence is 2.2 million per year
- Breast cancer mortality rates higher in developing countries

- Dose Schedule
- Volume Of Treatment
- Techniques Of Radiotherapy

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- Dose Schedule
- Volume Of Treatment
- Techniques Of Radiotherapy



- **Definition:** Delivers higher doses of radiation per session over a shorter period.
- Benefits: Comparable efficacy to conventional fractionation with reduced treatment duration and potential for fewer side effects.

• Evidence: Studies like the UK START trials have demonstrated similar local control and survival rates with HFRT compared to conventional fractionation [Haviland JS et al., Lancet Oncol. 2013].



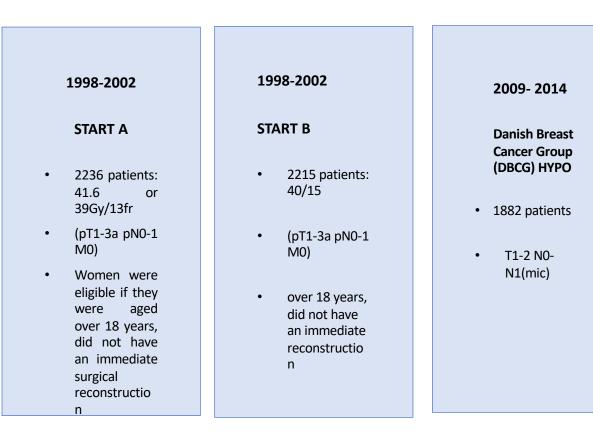
• A historical regimen of 25–28 fractions over 6 weeks was adopted for radiotherapy (RT) following breast-conserving surgery (BCS) and total mastectomy.

 An early assumption that breast cancer cell lines might be more sensitive to fractional doses than acute skin reactions and other squamous carcinomas led to development of the hypofractionated RT (HypoRT) approach which elevated fractional dose up to 3 Gy with reduced total dose/fractions, for obtaining radiobiological equivalence to a traditional regimen of 50–50.4 Gy/25-28f.



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Hypofractionated Radiation Therapy (HFRT)



29 January 2025



	START pilot	START A	START B	OCOG	Beijing	Chinese	MDACC	DBCG	TROG	
								Нуро	07.01	
Year	1986-1998	1998-2002	1999-2001	1993–1996	2008-2016	2010-2015	2011-2014	2009-2014	2007-2014	
n	1,410	2,236	2,215	1,234	820	734	287	1,854	1,608	
Standard arm ^{<u>a)</u>}	50 Gy/25 fx	50 Gy/25 fx	50 Gy/25 fx	50 Gy/25 fx	50 Gy/25 fx					
Test arm <u>a)</u>	42.9 Gy/13	41.6 Gy/13	40 Gy/15 fx	42.5 Gy/16	43.5 Gy/15 fx	43.5 Gy/15	42.5 Gy/16	40 Gy/15 fx	42.5 Gy/16	
	fx (5)	fx (5)	(3)	fx (3)	(3)	fx (3)	fx (3)	(3)	fx (3)	
	39 Gy/13 fx	39 Gy/13 fx								
	(5)	(5)								



	START pilot (50 Gy vs. 42.9	START A (50 Gy vs. 41.6 Gy vs.	(50 Gy vs	OCOG (50 Gy vs 42.5 Gy)			MDACC (50 Gy vs. 42.5 Gy)	DBCG Hypo (50 Gy vs. 40	TROG 07.01 (50 Gy vs.
	Gy vs. 39 Gy)	39 Gy)						Gy)	42.5 Gy)
Follow-up (yr) 5-yr IBTR	9.7	9.3	9.9	12	4.9	6.1	4.1	7.3	6.6
Standard	7.9	3.4	3.3	3.2	8.1 (LRR)	1.2	98 (LRFS)		5.1
Test	7.1	3.1	2	2.8	8.3 (LRR)	2	99 (LRFS)		5.1
	9.1	4.4							
10-yr IBTR									
Standard	12.1	6.7	5.2	6.7				3.3 (9-yr LRR)	
Test	9.6	5.6	3.8	6.2				3.0 (9-yr LRR)	
	14.8	8.1							

IBTR: Ipsilateral breast tumor relapse



 Given excellent IBTR control rates and toxicity profiles from existing data

HypoRT is an efficient, safe, and convenient treatment approach for breast cancer. The standard of care for adjuvant RT has shifted from 5–6 weeks of conventional fractionated RT to 3–4 weeks of HypoRT.



- Definition: Delivers higher doses of radiation per session over a shorter period.
- Benefits: Comparable efficacy to conventional and hypofractionation with reduced treatment duration and potential for fewer side effects.

 uHWBRT arose in centers that have logistics problems in treatment length and costs



UltrahypofractionatedRadiation Therapy (UHFRT)

1998-2002	1998-2002	2009- 2014	2004-2007	2011-2014
• 2236 patients: 41.6 or	START B 2215 patients: 40/15 	Danish Breast Cancer Group (DBCG) HYPO	FAST Trial	Fast-Forward Trial 4096 patients
39Gy/13fr • (pT1-3a pN0-1 M0) • Women were eligible if they	• (pT1-3a pN0-1 M0)	 1882 patients T1-2 N0- N1(mic) 	 915 women (pT1-2 pN0) Women ≥ 50 years of age 	 4096 patients (pT1-3, pN0-1, M0)
were aged over 18 years, did not have an immediate surgical reconstructio	 over 18 years, did not have an immediate reconstructio n 			 aged at least 18 years



	START pilot	START A	A START B OCOG Beijing		Beijing	Chinese	MDACC	DBCG	TROG	FAST	FAST-	
								Нуро	07.01		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 ^{<u>a)</u>}	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 ^{<u>a)</u>}	42.9 Gy/13	41.6 Gy/13	40 Gy/15 fx	42.5 Gy/16	43.5 Gy/15 fx	43.5 Gy/15	42.5 Gy/16	40 Gy/15 fx	42.5 Gy/16	30 Gy/5 fx	27 Gy/5 fx	
	fx (5)	fx (5)	(3)	fx (3)	(3)	fx (3)	fx (3)	(3)	fx (3)	(5)	(1)	
	39 Gy/13 fx	39 Gy/13 fx								28.5 Gy/5	26 Gy/5 fx	
	(5)	(5)								fx (5)	(1)	



	START pilot (50	START A (50 Gy vs.	(50 Gy vs		(50 Gy vs.		MDACC (50 Gy vs.			30 Gy vs. 28.5	FAST-Forward (40 Gy vs. 27 Gy vs. 26 Gy)
	Gy vs. 42.9 Gy vs. 39	41.6 Gy vs. 39 Gy)	40 Gy)	42.5 Gy)	43.5 Gy)	43.5 Gy)	42.5 Gy)	Gy vs. 40 Gy)	Gy vs. 42.5 Gy)	Gy)	
	Gy)	0 / Uyj						۵	1210 dy)		
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		0.7	
								LRR)			
Test	9.6	5.6	3.8	6.2				3.0 (9-yr		1.4	
								LRR)			
	14.8	8.1								1.7	

Ultra-hypofractionated whole breast adjuvant radiotherapy



-single experience with 271 patients treated with 3D and IMRT technique

 -T1-T3 invasive BC, no or limited axillary involvement, age ≥ 65 years or women with commuting difficulties or disabling diseases.

Ultra-hypofractionated whole breast adjuvant radiotherapy in the real-world setting : single experience with 271 elderly/frail patients treated with 3D and IMRT technique, Maria Alessia Zerella, Radiotherapy and Oncology, 2021 April -The only severe acute toxicity (G3) at the end of RT was erythema (0.4%), registered in the 3DCRT group. With 18 months of median follow-up, severe early-late toxicity (G3) was reported in terms of fibrosis and breast retraction, both with an incidence of 1.4%, mostly in the 3DCRT group.

-At 3 years, disease-free survival and overall survival were 94.9% and 97.8%, respectively

Ultra-Hypofractionation for Whole-Breast Irradiation in Early Breast Cancer: Interim Analysis of a Prospective Study

-A total of 70 patients were treated. Fiftynine were treated with the 26 Gy/5 fr/1 w and 11 with the 28.5 Gy/5 fr/5 ws schedule

-IMRT for all patients

-Median age was 67 and 70 in the two groups

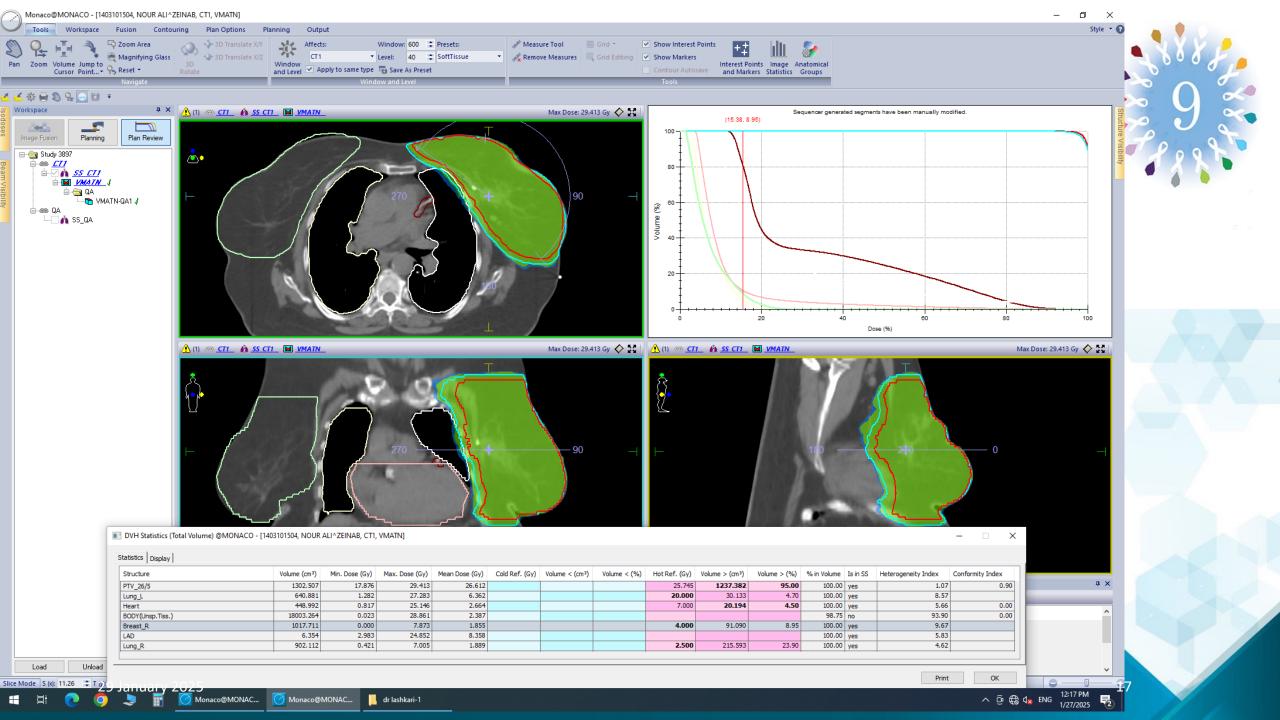
-Most of the patients had a clinical T1N0 disease

Ultra-Hypofractionation for Whole-Breast Irradiation in Early Breast Cancer: Interim Analysis of a Prospective Study, Valeria Sigaudi, Biomedicines 2022 oct



-Maximum detected acute skin toxicities were grade 2 erythema (6.7%), grade 2 induration (4.4%), and grade 2 skin colour changes

-No early IBTR was observed.



- Dose Schedule
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Accelerated partial breast irradiation (APBI)

• Patient selection

criteria

1	Age \geq 50 years
2	Tumor size ≤ 2 cm
3	Invasive non-specific type of cancer, infiltrative non-specific type of cancer
4	Grade I or II of malignancy
5	The absence of lymph node lesions and distant metasta- ses, NO and MO
6	Surgical margin: cancer not exposed, \geq 3 mm
7	Luminal A (ER+, PR+, Her2/neu+1) and luminal B (ER+/, PR+/, Her2/neu+1)
8	Negative results for mutations of BRCA genes
9	The Ki-67 ≤ 40%

Accelerated Partial Breast Irradiation for Early-Stage Invasive Lobular Carcinoma

- Of 1248 patients treated from 2010 to 2022 who underwent APBI, the study cohort comprised 132 (11%) who had ILC, either exclusively or mixed with another histology
- Median age 63/Median tumor size was 1.1 cm/ all ER positive disease (99%) and hormone therapy (91%)/sentinel node biopsy (89%) with the remainder having no axillary surgery.
- All patients received external beam APBI to 40 Gy in 10 daily fractions.
- Outcomes of interest included local recurrence (LR) and overall survival (OS).

- Results
- A median follow-up was 39 months
- 4-year LR rate of 3% (Both events arose in patients with mixed lobular histology (none arose in patients with pure ILC)
- No regional or distant recurrences were observed
- OS was excellent(98%)

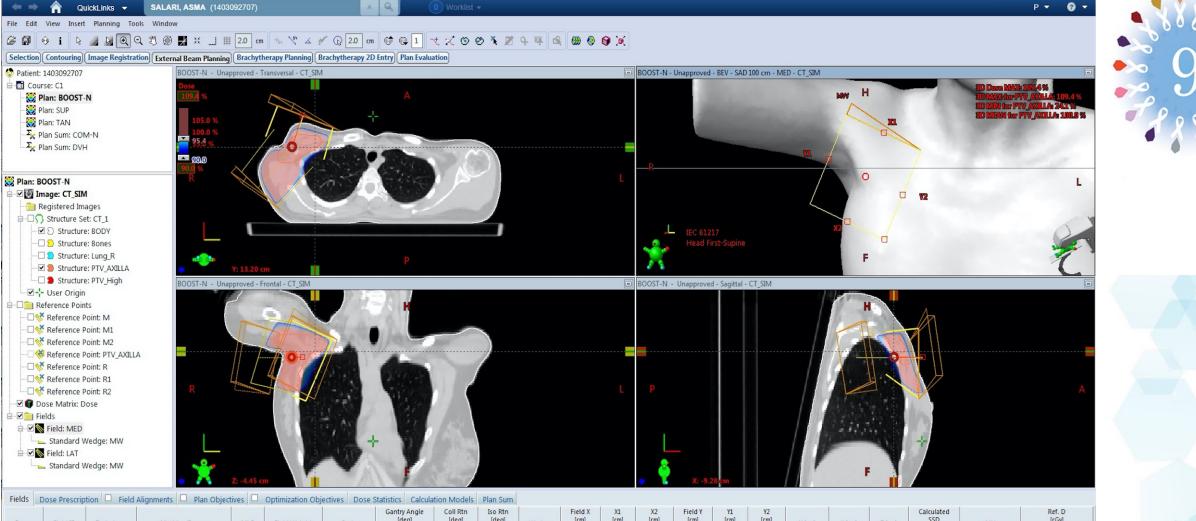


Accelerated Partial Breast Irradiation for Early-Stage Invasive Lobular Carcinoma ,Lior Z Braunstein, ijrobp 2024 oct

Axillary Boost



 In the population of patients with extranodal extension(ENE), the majority of failures are distant with no isolated LRFs. Locoregional failures are the highest in the IMN + ax/SCV group (~40%). treatment escalation should be considered for these patients.



Group	Field ID	Technique	Machine/Energy	MLC	Field Weight	Scale	[deg]	[deg]	[deg]	Wedge	[cm]	[cm]	(cm)	[cm]	(cm)	12 [cm]	X [cm]	Y [cm]	Z [cm]	SSD [cm]	MU	[cGy]
~	MED	STATIC-I	Elekta-Compact1 - 6X		1.100	IEC61217	20.0	246.0	0.0	MW	10.0	-5.0	+5.0	9.0	-4.5	+4.5	-12.89	12.29	-4.45	96.4	O: 91 W: 99	O: 95.9 W: 23.8
~	LAT	STATIC-I	Elekta-Compact1 - 6X		0.900	IEC61217	222.0	104.0	0.0	MW	10.0	-5.0	+5.0	8.0	-4.0	+4.0	-12.89	12.29	-4.45	92.9	O: 84 W: 91	O: 94.5 W: 23.2

- Dose Schedule
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Radiotherapy Techniques

- IMRT
- VMAT
- Proton beam
- SBRT
- DIBH





Intensity-Modulated Radiation Therapy (IMRT)

• Definition: Uses advanced technology to modulate the radiation dose, conforming to the shape of the tumor

 Benefits: Allows for higher doses to the tumor while sparing normal tissues, potentially reducing side effects.

29 January 2025

Comparative Effectiveness Analysis of 3D-Conformal Radiation Therapy Versus Intensity Modulated Radiation Therapy (IMRT) in a Prospective Multicenter Cohort of Patients With Breast Cancer(university of Michigan)

Conventional fractions

-1185 patients treated with 3DCRT

650 (54.9%) experienced acute toxicity (moderatesevere pain or moist desquamation)

-774 treated with highly segmented forward-planned IMRT, 458 (59.2%) experienced acute toxicity

-580 treated with inverse-planned IMRT, 245 (42.2%) experienced acute toxicity

Hypofraction

 1296 patients treated with 3DCRT, 432 (33.3%) experienced acute toxicity

-709 treated with highly segmented forward-planned IMRT, 227 (32.0%) experienced acute toxicity

-623 treated with inverse-planned IMRT, 164 (26.3%) experienced acute toxicity

study found a significant benefit from inverse-planned IMRT compared with 3DCRT in reducing acute toxicity of breast radiation therapy

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Comparative Effectiveness Analysis of 3D-Conformal Radiation Therapy Versus Intensity Modulated Radiation Therapy (IMRT) in a Prospective Multicenter Cohort of Patients With Breast Cancer, Reshma Jagsi MD et al, International Journal of Radiation Oncology*Biology*Physics Volume 112, Issue 3, 1 March 2022

IMRT in patients with Immediate prosthesis implantation after mastectomy

-104 patients undergoing IMRT after MRM for breast cancer

-Radiotherapy was performed on the ipsilateral chest wall, supraclavicular and infraclavicular lymph nodes at a dose of 50Gy/2Gy/25f.)

The patients were divided into two groups according to whether undergoing breast reconstruction.

-first group, all patients underwent immediate implant-based breast

-Patients in the second group received modified radical mastectomy without breast reconstrution.

- The first group was named IBBR group with 46 patients.
- The second group was named nonreconstruction group with 58 patients
- Radiotherapy dosimetry and radiotherapy related complications of immediate implant-based reconstruction after breast cancer surgery Yu Zhang et al, frontiers in oncology,2023 oct



- grade1-2 capsular contracture occurred in17.4% patients in the IBBR group
- wound infection occurred in 11.0%
- skin necrosis occurred in 6.5%
- No implant rupture occurred
- implant loss occurred in two patients after completion of radiotherapy due to infection, and the reconstruction failure rate was 4.3%

With the advancement of radiotherapy technology,IBBR is a reasonable option for patients who need radiotherapy after modified radical mastectomy.





Volumetric-Modulated Arc Therapy (VMAT)

 Definition: Uses advanced technology to modulate the radiation dose, conforming to the shape of the tumor

 Benefits: A rotational form of IMRT and allows for higher doses to the tumor while sparing normal tissues, potentially reducing side effects. Three-dimensional conformal radiotherapy (3D-CRT) vs. volumetric modulated arc therapy (VMAT)

-All plans fulfilled the criterium for PTV V95%≥ 95%.

-The PTV coverage, homogeneity, and conformity indices were significantly better for VMAT-DIBH.

- VMAT showed a significantly increased mean dose and V5Gy for all OARs, but reduced LAD Dmax by 15 Gy.
- For ipsilateral and contralateral lung and contralateral breast, the 3D-CRT DIBH method achieved the lowest values of Excess absolute risks

The study shows that VMAT-DIBH provides better OAR sparing against high doses.
 The large low-dose-bath (≤5 Gy) is still a concern due to the fact that a larger volume of normal tissues exposed to lower doses may increase a radiation-induced risk of secondary cancer.

Three-dimensional conformal radiotherapy (3D-CRT) vs. volumetric modulated arc therapy (VMAT) in deep inspiration breath-hold (DIBH) technique in left-sided breast cancer patients—comparative analysis of dose distribution and estimation of projected secondary cancer risk Iga Racka et al,Strahlenther Onkol,2022 July



VMAT vs IMRT

- VMAT plans significantly reduced treatment time and MU number when compared with IMRT in patients of left-sided breast cancer after modified radical mastectomy
- VMAT were associated with slightly advantage in terms of heart and coronary arteries sparing.
- Similar PTV coverage and sparing of other normal tissues were observed between these 2 techniques.

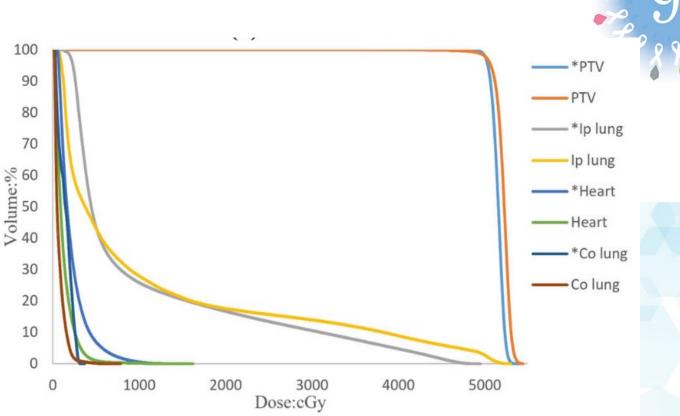
Dosimetric comparison between intensity modulated radiotherapy and volumetricmodulated arc therapy in patients of left-sided breast cancer treated with modified radical mastectomy,<u>Rui Wang et al,Medicine (Baltimore). 2022 Jan</u> VMAT is a promising technique in the treatment of left-sided breast cancer



Comparison of plan quality between VMAT and IMRT for breast cancer

Breast conserving surgery: (a)

- *V* 50Gy of PTV for both IMRT and VMAT are 98%, but the homogeneity of the VMAT plan is better than that of the IMRT plan.
- For the ipsilateral lung, V 20Gy, V 30Gy, and mean dose of VMAT plan are better than those of IMRT plan, and V 5Gy is slightly higher.
- The doses to heart and contralateral lung of the VMAT plan are higher than those of the IMRT plan, but they are far less than the dose limitation.

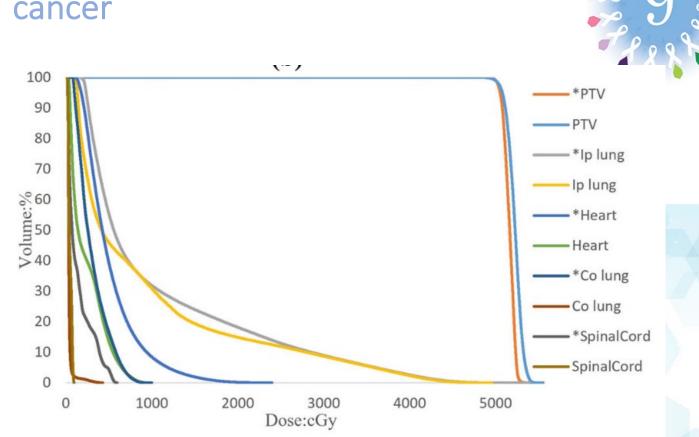


Comparison of plan quality and robustness using VMAT and IMRT for breast cancer, Chuou Yin et al, the journal <u>Open Physics 2024</u>

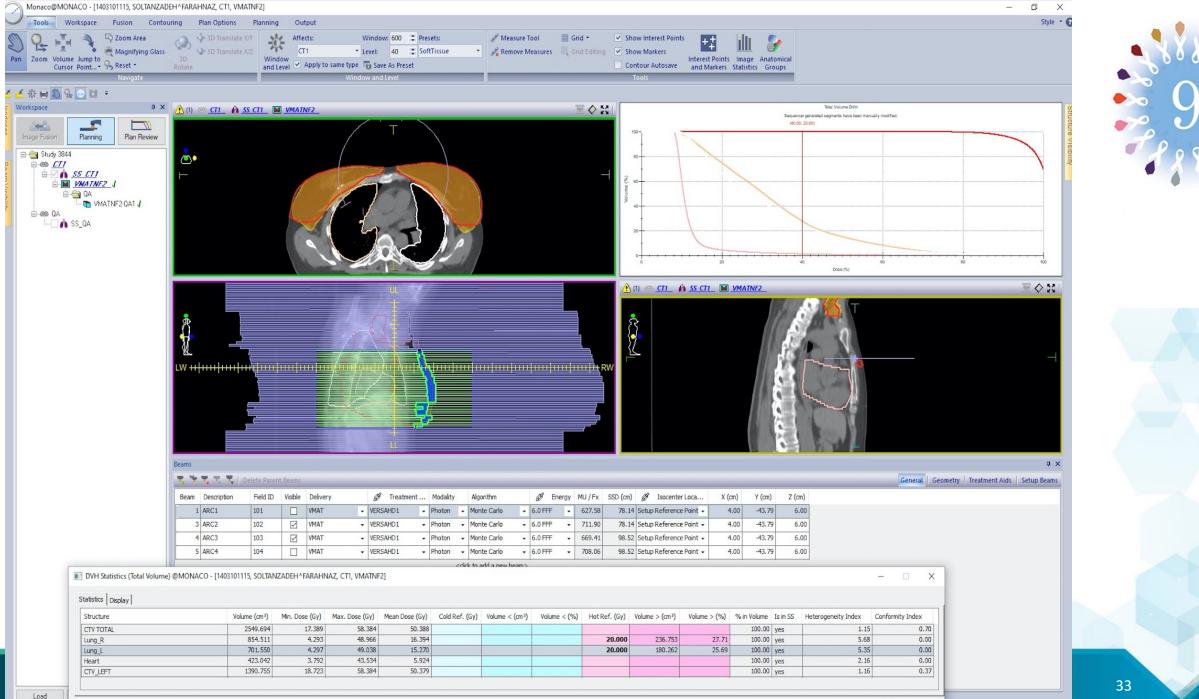
Comparison of plan quality between VMAT and IMRT for breast

Post mastectomy: (b)

- The V 50Gy of PTV for VMAT plan and IMRT plan are 99.1 and 99.0%, respectively. The homogeneity of the VMAT plan is better than the IMRT plan.
- For the ipsilateral lung, the volume of VMAT plan is higher than that of IMRT plan when the dose is less than 1,000 cGy. However, the opposite result is found when the dose is between 1,000 and 3,000 cGy. In the high-dose region (>3,000 cGy), the DVH curves of the two plans almost overlapped.
- The doses to heart, contralateral lung, and spinal cord in VMAT plan are higher than those in IMRT plan, but they are lower than their dose limitations.



Comparison of plan quality and robustness using VMAT and IMRT for breast cancer, Chuou Yin et al, the journal <u>Open Physics ,2024</u>



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Proton Beam Therapy (PBT)

• Definition: Uses protons instead of X-rays, allowing for more precise targeting of tumors

• Benefits: Reduced radiation dose to surrounding normal tissues, potentially lowering the risk of side effects.



Evidence: Emerging data suggest benefits in reducing cardiac and lung exposure, particularly in left-sided breast cancer [MacDonald SM et al., Int J Radiat Oncol Biol Phys. 2013]

Stereotactic Body Radiation Therapy (SBRT)

- Definition: Delivers very high doses of radiation in a few fractions with high precision.
- Benefits: Potential for shorter treatment courses and improved local control in selected oligometastatic cases.

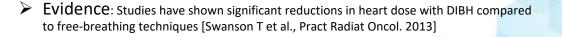
Evidence: Preliminary studies suggest SBRT may be effective for oligometastatic breast cancer, though more research is needed [Navarria P et al., Breast. 2018]





Deep Inspiration Breath Hold (DIBH):

- Definition: A technique where patients hold their breath during radiation delivery to increase the distance between the heart and the chest wall.
- Benefits: Reduces radiation exposure to the heart, decreasing the risk of cardiac toxicity.





Artificial Intelligence in Radiotherapy

- Title: AI is Enhancing Treatment Precision
- Content: Artificial intelligence is being utilized to improve imaging quality and enable real-time adjustments during radiotherapy, minimizing damage to healthy tissues and enhancing treatment outcomes.

1. Precision and Personalization:

- AI can enhance the precision of radiation therapy by improving tumor targeting and sparing healthy tissues. This is achieved through advanced imaging analysis and treatment planning algorithms.

- Personalized treatment plans can be developed by integrating patient-specific data, leading to potentially better outcomes and reduced side effects.

2. Efficiency and Workflow:

- AI can streamline the workflow in radiation oncology by automating routine tasks such as contouring of organs at risk and treatment planning, thereby reducing the workload on clinicians and minimizing human error.

3. Adaptive Radiation Therapy:

 AI can facilitate adaptive radiation therapy, where treatment plans are adjusted in real-time based on changes in tumor size, shape, and position during the treatment course.





Adding Immunotherapy to Radiation Therapy

1. Rationale:

- Combining immunotherapy with radiation therapy (RT) can potentially enhance the anti-tumor immune response. RT can increase the release of tumor antigens, which may be more effectively targeted by the immune system when combined with immunotherapy.

2. Clinical Evidence:

- Studies have shown that combining RT with immune checkpoint inhibitors (e.g., pembrolizumab, nivolumab) can improve outcomes in certain cancers, including breast cancer. This combination can lead to a synergistic effect, enhancing both local and systemic tumor control.

3.Clinical Trials:

- Ongoing clinical trials are investigating the efficacy and safety of combining RT with various immunotherapies in breast cancer. These trials aim to determine optimal dosing, timing, and sequencing of treatments to maximize therapeutic benefits while minimizing adverse effects.

Considerations and Challenges

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1. Patient Selection:

 Not all patients may benefit equally from the combination of RT and immunotherapy. Biomarkers and genetic profiling can help identify patients

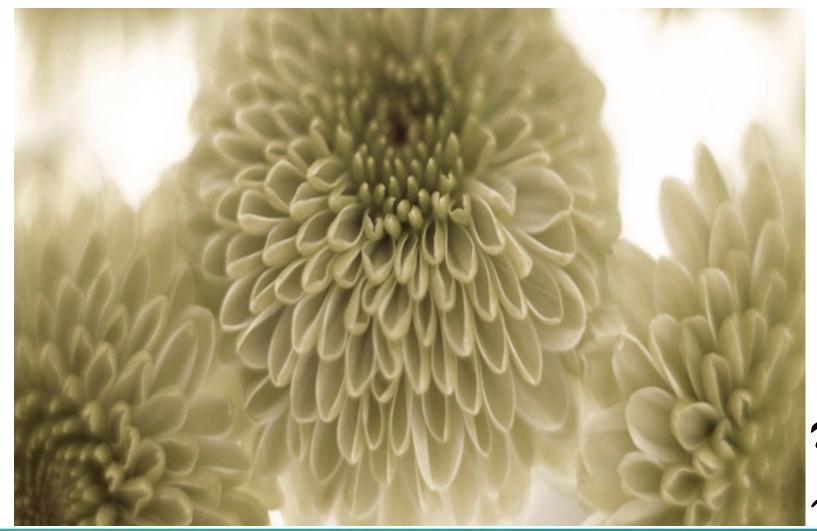
2. Toxicity Management:

- Combining RT with immunotherapy can increase the risk of immunerelated adverse events. Close monitoring and management of these toxicities are crucial to ensure patient safety.





- Advancements in radiation therapy for breast cancer, such as HFRT, APBI, PBT, DIBH, IMRT, and SBRT, offer promising options for improving treatment efficacy and reducing side effects.
- Ongoing research and clinical trials continue to refine these techniques, aiming to optimize outcomes for breast cancer patients.
- Al-assisted radiation therapy and the addition of immunotherapy to radiation therapy hold promise for improving outcomes in breast cancer treatment. However, careful consideration of patient selection, toxicity management, and cost is essential for the successful implementation of these advanced therapies.





Thanks for Your Attention