Surface Guided Deep Inspiration Breath Hold in Ultra-hypofractionated Radiotherapy for Early Stage Left Breast Cancer: a Single-Centre Analysis

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INTRODUCTION

- Surface Guided Radiation Therapy (SGRT) effectively assesses, monitors and checks patient set-up in real-time
- Exposure to ionising radiation is eliminated
- The system is being introduced more and more into clinical practice across several techniques and irradiation-sites

INTRODUCTION

Perugia Radiation Oncology Centre has been using SGRT with the AlignRT® System (*VisionRT, London, UK*) since 2020

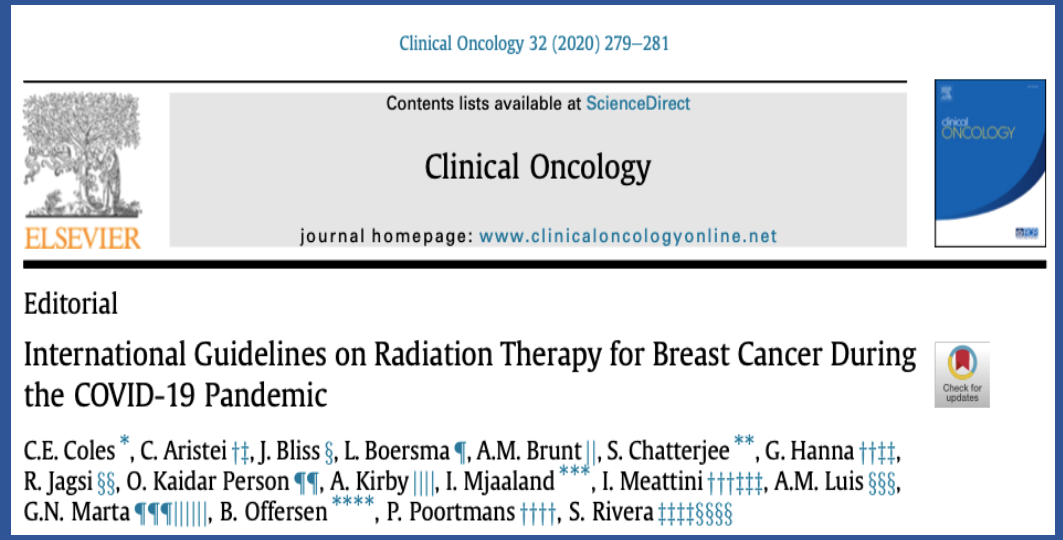
Our radiation oncologists, medical physicists and radiation therapy technicians learnt the necessary skills very quickly

We are using it in breast cancer patients and, occasionally, in head and neck cancer patients

INTRODUCTION

In April 2020 we adopted an ultra-hypofractionated schedule (26 Gy in 5 consecutive fractions) for whole breast irradiation (WBI) after conserving surgery

Ultra-hypofractionation was recommended to reduce the risk of COVID-19 infection in patients and health-care professionals



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Editorial

International Guidelines on Radiation Therapy for Breast Cancer During the COVID-19 Pandemic

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INTRODUCTION

Ultra-hypofractionation and tumour control

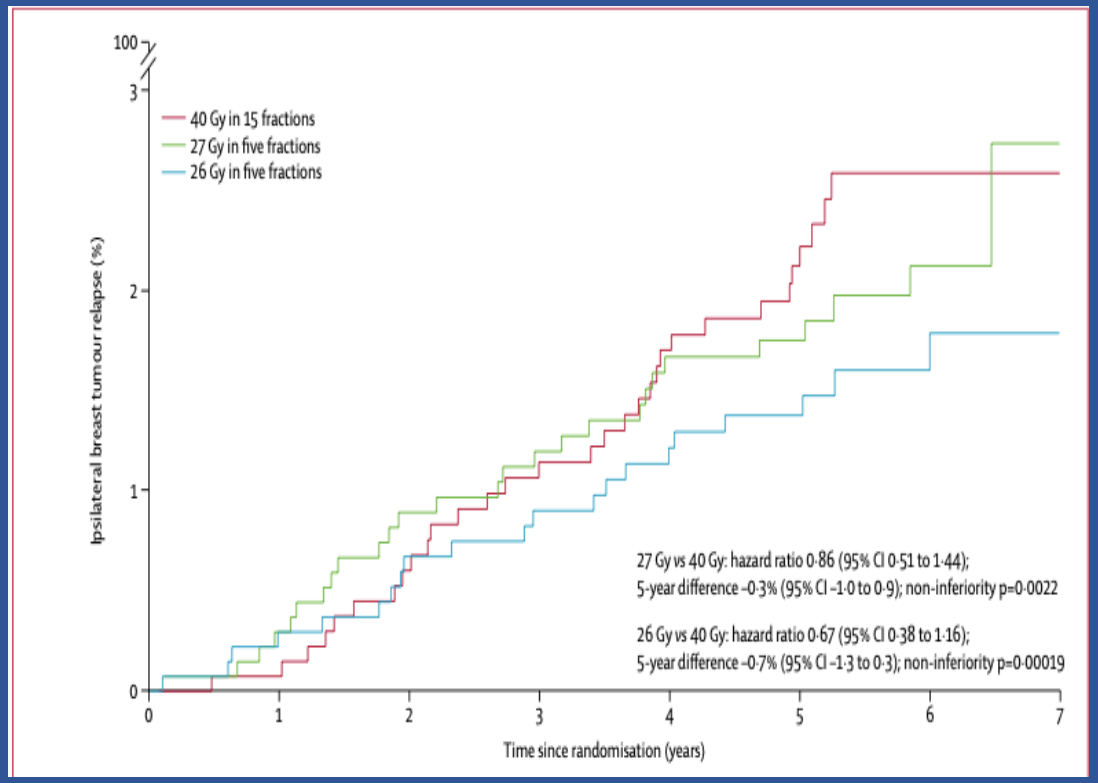
Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial

Adrian Murray Brunt, Joanne S Haviland*, Duncan A Wheatley, Mark A Sydenham, Abdulla Alhasso, David J Bloomfield, Charlie Chan, Mark Chum, Susan Cleator, Charlotte E Coles, Andrew Goodman, Adrian Hamett, Penelope Hopwood, Anna M Kirby, Chona 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*

www.thelancet.com **Published online April 28, 2020 https://doi.org/10.1016/S0140-6736(20)30932-6**

4,096 patients with invasive breast carcinoma (pT1–3, pN0–1) were enrolled

Tumour control: The five-fraction schedules were not inferior to 40 Gy in 15 fractions



INTRODUCTION

Ultra-hypofractionation and side effects

97% of patients had at least one annual clinical assessment of normal tissue effects

Any moderate/marked clinician-assessed side effect was observed in:

9.9% with 40 Gy

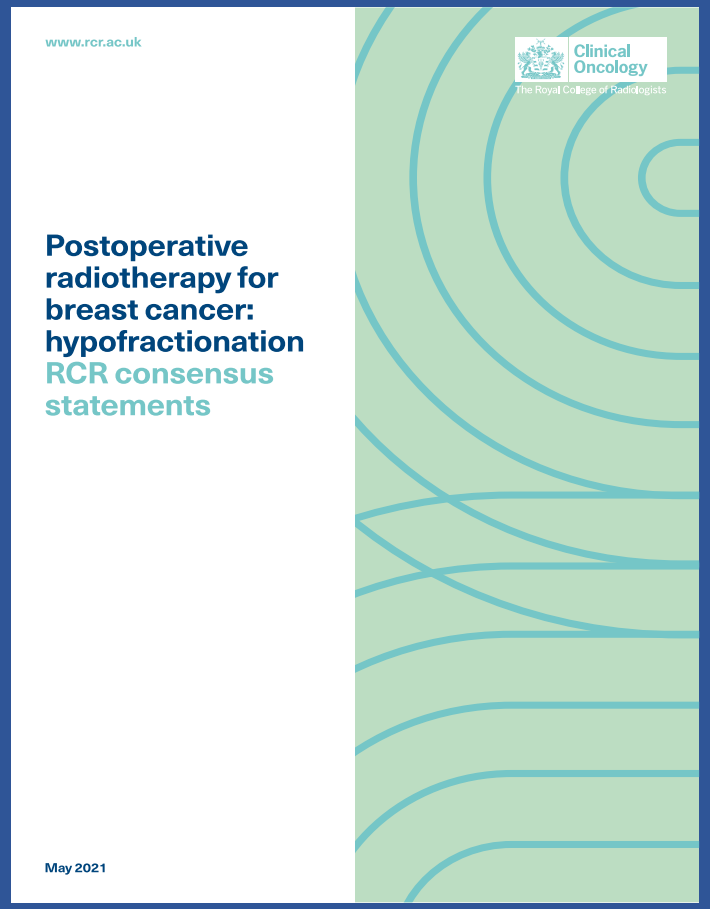
15.4% with 27 Gy

11.9% with 26 Gy

26 Gy schedule was recommended

Ultra-hypofractionation and side effects

	Number of moderate or marked events/total number of assessments over follow-up	Odds ratio for schedule (95% CI)	p value for comparison with 40 Gy	p value for comparison between 27 Gy and 26 Gy	Odds ratio for years of follow-up (95% CI); p value
Any adverse event in the breast or chest wall*	..	..	..	..	0·98 (0·96–1·00); 0·055
40 Gy	651/6121 (10·6%)	1 (ref)	..	..	..
27 Gy	1004/6303 (15·9%)	1·55 (1·32–1·83)	<0·0001	..	..
26 Gy	774/6327 (12·2%)	1·12 (0·94–1·34)	0·20	0·0001	..
Breast distortion†	..	..	..	..	0·99 (0·95–1·02); 0·38
40 Gy	232/5724 (4·0%)	1 (ref)	..	..	..
27 Gy	363/5953 (6·1%)	1·51 (1·15–1·97)	0·0028	..	..
26 Gy	299/5945 (5·0%)	1·20 (0·91–1·60)	0·19	0·083	..
Breast shrinkage†	..	..	..	..	1·03 (1·00–1·06); 0·023
40 Gy	330/5728 (5·8%)	1 (ref)	..	..	..
27 Gy	503/5944 (8·5%)	1·50 (1·20–1·88)	0·0004	..	..
26 Gy	369/5943 (6·2%)	1·05 (0·82–1·33)	0·71	0·0018	..
Breast induration (tumour bed)†	..	..	..	..	1·00 (0·96–1·04); 0·95
40 Gy	185/5713 (3·2%)	1 (ref)	..	..	..
27 Gy	304/5948 (5·1%)	1·56 (1·19–2·05)	0·0013	..	..
26 Gy	236/5937 (4·0%)	1·19 (0·90–1·59)	0·23	0·047	..
Breast induration (outside tumour bed)†	..	..	..	..	0·96 (0·90–1·02); 0·17
40 Gy	45/5712 (0·8%)	1 (ref)	..	..	..
27 Gy	137/5943 (2·3%)	2·79 (1·74–4·50)	<0·0001	..	..
26 Gy	97/5930 (1·6%)	1·90 (1·15–3·14)	0·013	0·059	..
Telangiectasia	..	..	..	..	1·21 (1·14–1·29); <0·0001
40 Gy	63/6087 (1·0%)	1 (ref)	..	..	..
27 Gy	100/6272 (1·6%)	1·68 (1·07–2·65)	0·025	..	..
26 Gy	102/6300 (1·6%)	1·53 (0·96–2·43)	0·070	0·65	
Breast or chest wall oedema	..	..	..	..	0·73 (0·69–0·78); <0·0001
40 Gy	89/6097 (1·5%)	1 (ref)	..	..	..
27 Gy	217/6287 (3·4%)	2·18 (1·57–3·03)	<0·0001	..	..
26 Gy	155/6318 (2·4%)	1·47 (1·03–2·09)	0·032	0·0097	..
Breast or chest wall discomfort	..	..	..	..	0·93 (0·89–0·97); 0·0003
40 Gy	234/6086 (3·8%)	1 (ref)	..	..	..
27 Gy	269/6285 (4·3%)	1·10 (0·86–1·40)	0·44	..	..
26 Gy	250/6309 (4·0%)	0·98 (0·76–1·26)	0·86	0·35	..



Consensus statement 1

Statement	Voting outcome
Offer 26 Gy in five fractions over one week for whole breast radiotherapy.	Very strongly supported

European Society for Radiotherapy and Oncology Advisory Committee in Radiation Oncology Practice consensus recommendations on patient selection and dose and fractionation for external beam radiotherapy in early breast cancer

Icro Meattini, Carlotta Becherini, Liesbeth Boersma, Orit Kaidar-Person, Gustavo Nader Marta, Angel Montero, Birgitte Vrou Offersen, Marianne C Aznar, Claus Belka, Adrian Murray Brunt, Samantha Dicuonzo, Pierfrancesco Franco, Mechthild Krause, Mairead MacKenzie, Tanja Marinko, Livia Marrazzo, Ivica Ratosa, Astrid Scholten, Elżbieta Senkus, Hilary Stobart, Philip Poortmans, Charlotte E Coles**

High-quality randomised clinical trials testing moderately fractionated breast radiotherapy have clearly shown that *Lancet Oncol* 2022; 23: e21–31

	Consensus agreement	Strength
1. Whole breast irradiation		
1a. Moderate hypofractionated whole breast irradiation should be offered regardless of:		
I. Age at breast cancer diagnosis	91·3%	Strong consensus
II. Pathological tumour stage	91·3%	Strong consensus
III. Breast cancer biology	91·3%	Strong consensus
IV. Surgical margins status	100%	Unanimous consensus
V. Tumour bed boost	100%	Unanimous consensus
VI. Breast size	91·3%	Strong consensus
VII. Invasive or pre-invasive DCIS disease	91·3%	Strong consensus
VIII. Oncoplastic breast conserving surgery	91·3%	Strong consensus
IX. Use of systemic therapy	95·6%	Strong consensus
1b. Ultrahypofractionated (26 Gy in five fractions) whole breast irradiation can be offered as (1) standard of care or (2) within a randomised controlled trial or prospective registration cohort	86·9%	Consensus

https://doi.org/10.1007/s11547-022-01563-9
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POSITION PAPER

The Italian Association for Radiotherapy and Clinical Oncology (AIRO) position statements for postoperative breast cancer radiation therapy volume, dose, and fractionation

Icro Meattini[1,2] · Isabella Palumbo[3] · Carlotta Becherini[2] · Simona Borghesi[4] · Francesca Cucciarelli[5] · Samantha Dicuonzo[6] · Alba Fiorentino[7] · Ruggero Spoto[8] · Philip Poortmans[9,10] · Cynthia Aristei[3] · Lorenzo Livi[1,2]

Position statements

a. *Hypofractionation is considered standard of care for all indication of external-beam postoperative breast cancer radiation therapy, regardless of the number and size of target volumes and breast reconstruction.* Hypofractionation is standard of care both for invasive and ductal carcinoma in situ of the breast. There is no reason to prescribe irradiation schedules using more than 15–16 fractions [1–6].

b. *50 Gy in 25 fractions is no longer considered being standard of care.* It should be restricted to highly selected cases, such as concomitant chemoradiation and hyperthermia to enhance the radio-sensitisation effects of the combined systemic or local agents [3, 4].

c. *5-fraction whole breast and/or chest wall irradiation without reconstruction (26 Gy in 5 fractions) is considered standard of care.* This schedule it is not to be considered experimental and should be considered the preferred option especially (but not exclusively) in patients fulfilling the inclusion criteria of the FAST-Forward trial [1, 7–9].

d. *Moderate hypofractionation should be offered for regional nodal irradiation* [1, 3, 4, 6]. Postmastectomy hypofractionated radiation therapy is non-inferior to and had similar toxicities to conventional fractionated radiation therapy in patients with high-risk breast cancer [6].

Our First Experience with the AlignRT® System

When starting with the ultra-hypofractionated schedule and the AlignRT® System internal validation was our main aim

- We assessed set-up errors with the AlignRT® System

and

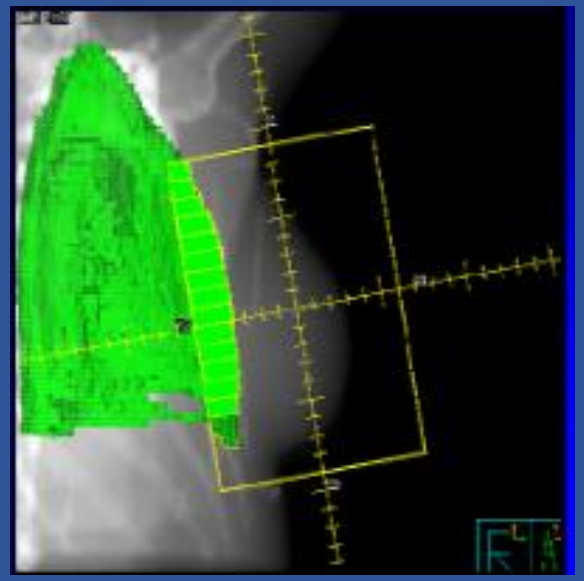
- Compared it with our standard radiological check system (co-registration of DRRs with 2D kV-portal images -PI-DRR-)

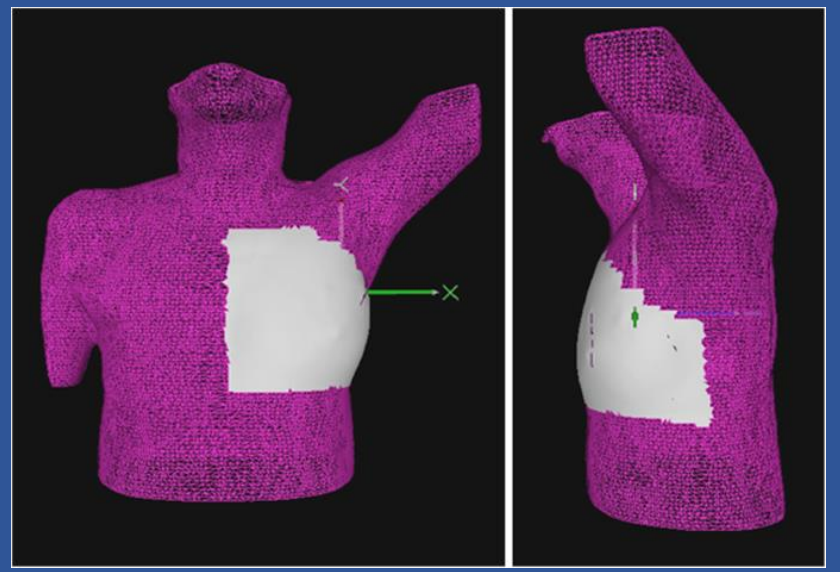
Significant differences emerged between AlignRT® and PI-DRR in the y (cranio-caudal; p=0.02) and z (antero-posterior; p=0.04) dimensions

We hypothesized the differences were due to:

- Inter-observer variability in portal imaging evaluation
- Different registration systems

PI-DRR is based on bone and SGRT on body surface





In 20 patients all set-ups with both SGRT and PI-DRR showed ≤ 5 mm deviation from the isocentre except for 1 outlier of -7 mm in the y dimension

The SGRT system emerged as reliable and reproducible and therefore suitable for routine practice

Our Second Experience with the AlignRT® System

- In April 2023 a new AlignRT® System entered into use in our centre
- It was equipped with a deep inspiration breath hold (DIBH) system

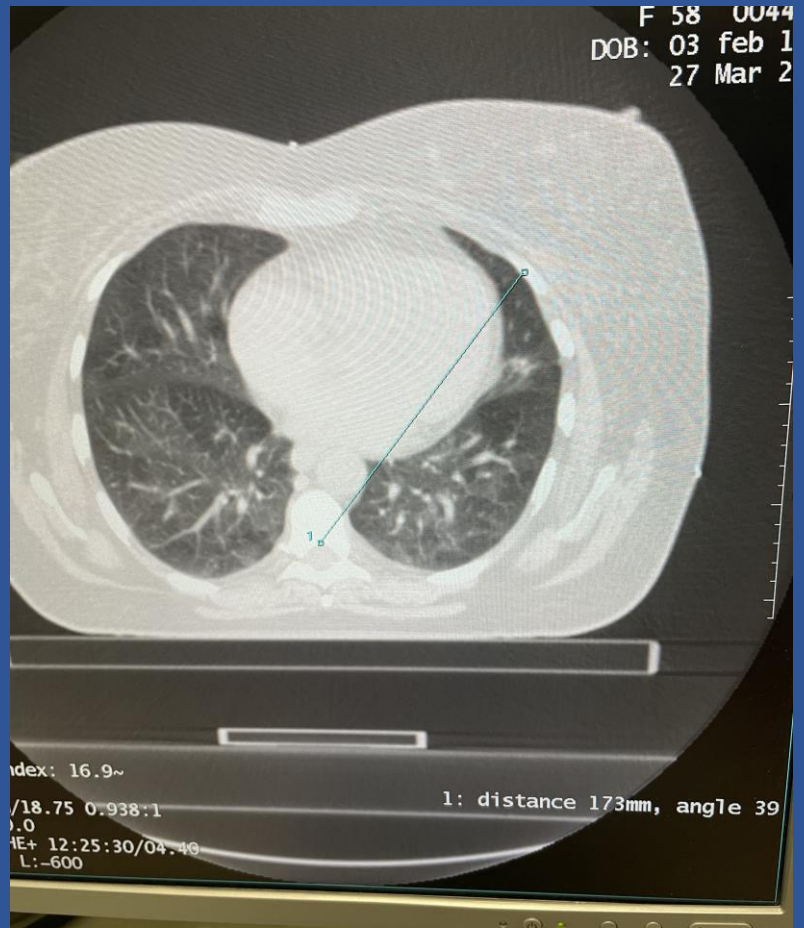
- We decided to test the system in all left side breast cancer patients who would be treated with the 5-fraction schedule so as to lower the dose to the heart

- To date, it has been used in 35 patients

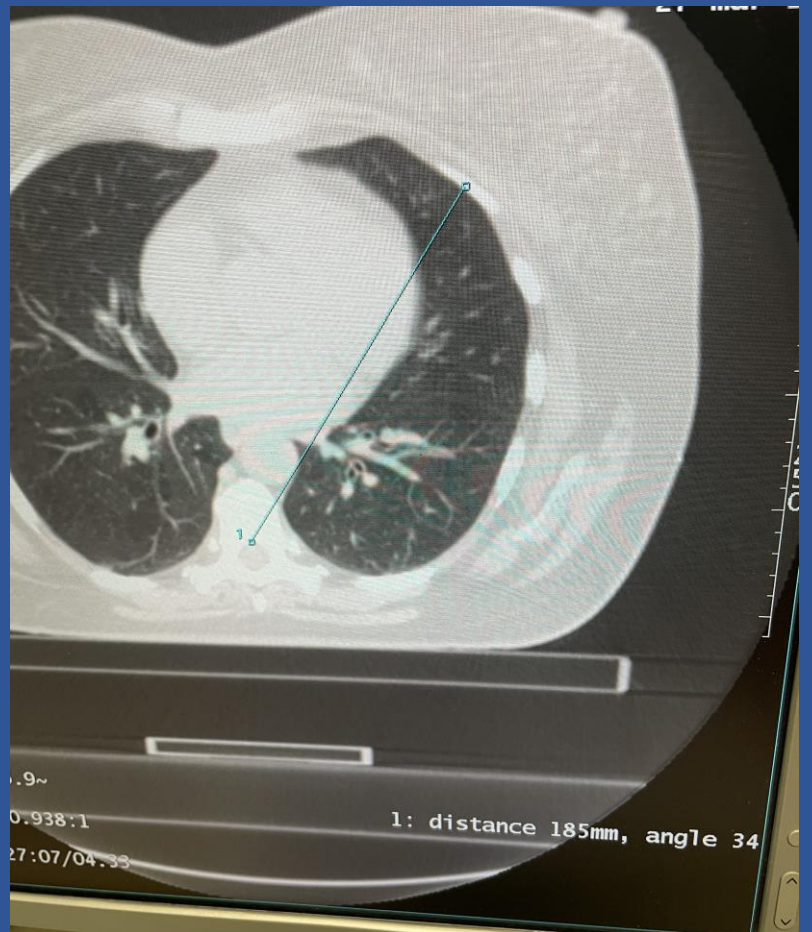
METHOD AND MATERIALS

2 CT scans were acquired

in free breath
for surface reference and tattoo alignment



in deep inhalation



METHOD AND MATERIALS

Contouring and Treatment Planning

As no regional lymph nodes were irradiated, a 3D technique was used for all patients

METHOD AND MATERIALS

In the first 10 patients we evaluated

dosimetric parameters

treatment delivery

patient compliance

METHOD AND MATERIALS

Dose Objectives for all Regions of Interest

ROI	Dx	Vx	Vx	Dmax	Dmean
Breast PTV	D95% ≥ 95%	V105% < 5%	V107% < 2%	Dmax < 110%	
Left lung		V8Gy < 15%			
Heart		V1.5Gy <30%	V7Gy < 5%		
LADCA					<6Gy

Murray Brunt et al., Lancet 2020
Piroth et al., Strahlenther Onkol 2019

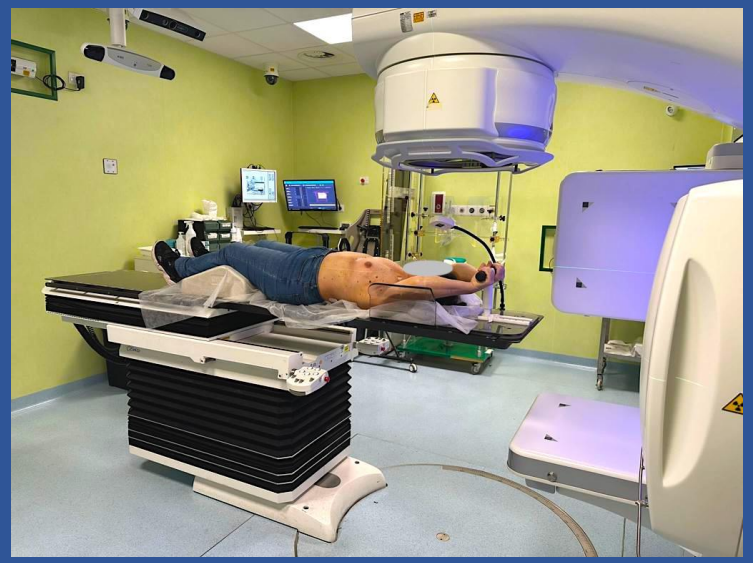
RESULTS

Dosimetric Parameters

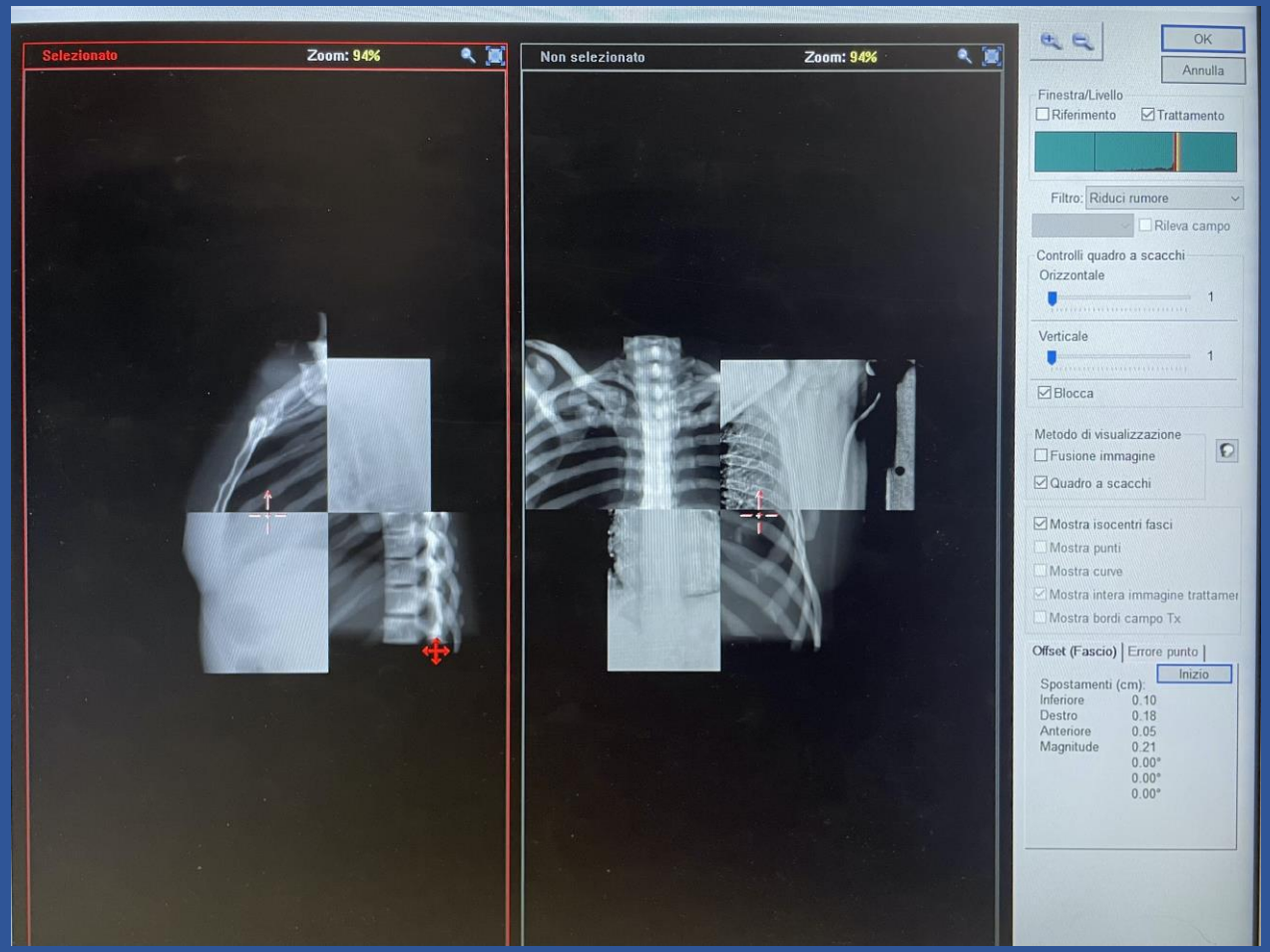
DIBH and FB plans were compared

ROI	Objective	DIBH	FB	p
Left lung	V8Gy < 15%	11.7%±1.6	13.6%±1.5	= 0.007
Heart	V1.5Gy <30% V7Gy < 5%	6.6%±5.4 0.5% ±0.5	12.8%±7.3 3.1%±2.1	= 0.005 = 0.008
LADCA	Dmean <6Gy	2.9Gy±1.5	7.3Gy±4.2Gy	= 0.005

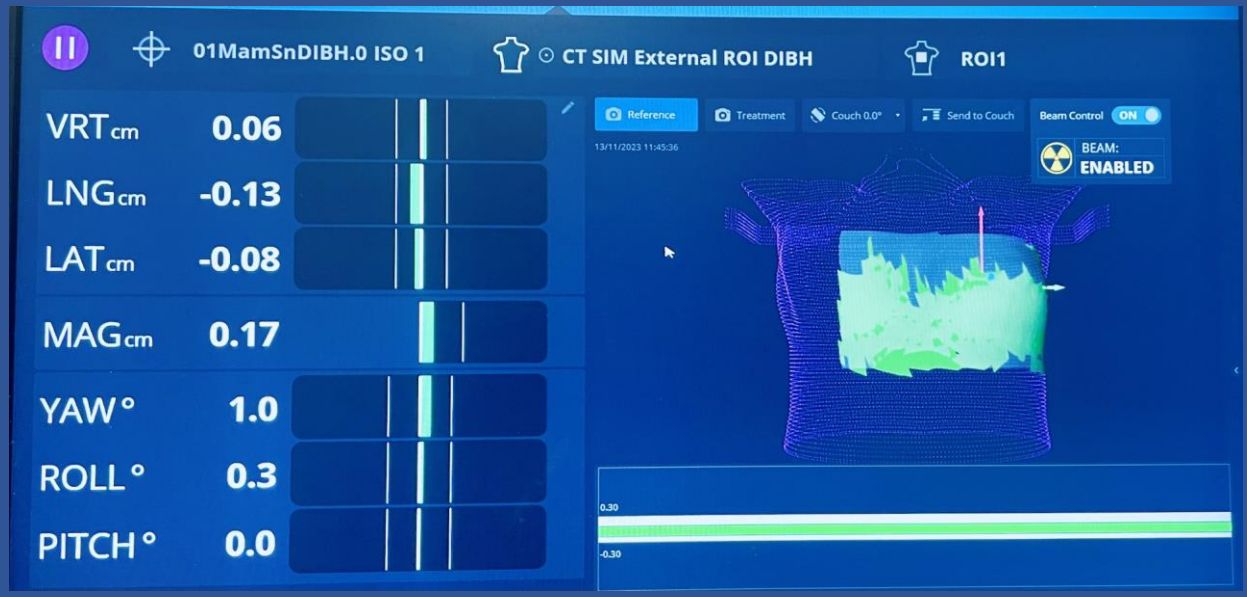
RESULTS
Treatment delivery



RESULTS
Treatment delivery



RESULTS
Treatment delivery



RESULTS

Treatment Delivery

The mean maximum shift in all directions, as calculated after co-registration of DRRs with PI, was <5 mm for all 10 patients

RESULTS

Patient Compliance

- All patients completed RT
- Compliance was very good

CONCLUSIONS

- SG-DIBH with AlignRT® System was valid
- Treatment delivery was reliable and reproducible
- Doses to the left lung, heart and LADCA were significantly reduced *vs* FB-WBI
- Maximum reduction was 84% for the heart V7Gy.

CONCLUSIONS

- At present SG-DIBH is part of our routine practice
- Our guide to standard SG-DIBH procedures is available online for our staff
- Work is in progress to confirm our preliminary results in a larger cohort

CONCLUSIONS

We consider SG-DIBH for all compliant left-sided breast cancer patients whether receiving ultra- or moderate- hypofractionated schedules

How do we identify who may benefit from it ?

- The CT scans indicate which candidates will benefit from SG-DIBH
- Treatment plans will confirm candidacy or not

Way Forward

- We are now aiming at shortening set-up times by reducing the number of PI-DRR, thus exposing the patient to less irradiation
- We expect to extend SG-DIBH to patients needing lymph node irradiation
- We might even see whether tattoos can be eliminated