



Brigham and Women's Hospital

Founding Member, Mass General Brigham

Hot Topics in Radiation Oncology Novel Technologies in Precision Oncology: Stereotactic Body Radiation Therapy

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Harvard Radiation Oncology Program Residency Program Director
Dually trained in Radiation Oncology and Palliative Medicine
Director, Skeletal Radiation Oncology
- Clinical focus: Spine metastatic disease
 - Research focus: Spine and non-spine bone metastases, palliative care in radiation oncology



DISCLOSURES

No relevant disclosures



OBJECTIVES

1. To gain familiarity with the technology of stereotactic body radiation therapy (SBRT) as a tool in the treatment of cancer
2. To understand the primary applications of SBRT in the treatment of primary and metastatic cancers



1. What is stereotactic body radiation therapy (SBRT)?

SBRT is the use of:

- ***precision set up and imaging** for RT planning and delivery (e.g., CT, MRI, dynamic CT and MRI)*
- ***with computer-based inverse algorithms for highly conformal RT planning and delivery***
- ***to achieve high dose per treatment, ablative doses of RT, with sharp dose fall off** resulting in minimal dose to surrounding nearby normal tissues*
- ***typically delivered in 1 to 5 treatment sessions** given daily or every other day*



1. What is stereotactic body radiation therapy (SBRT)?



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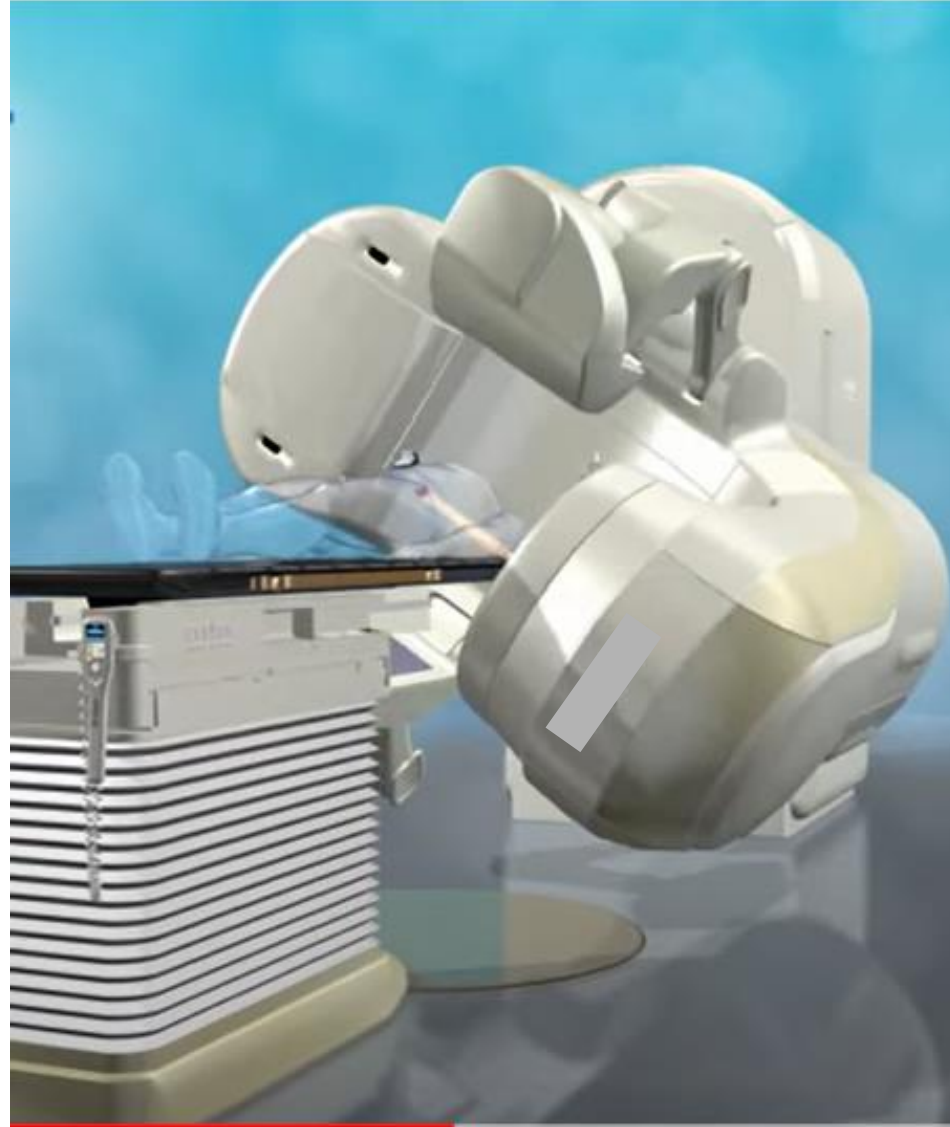
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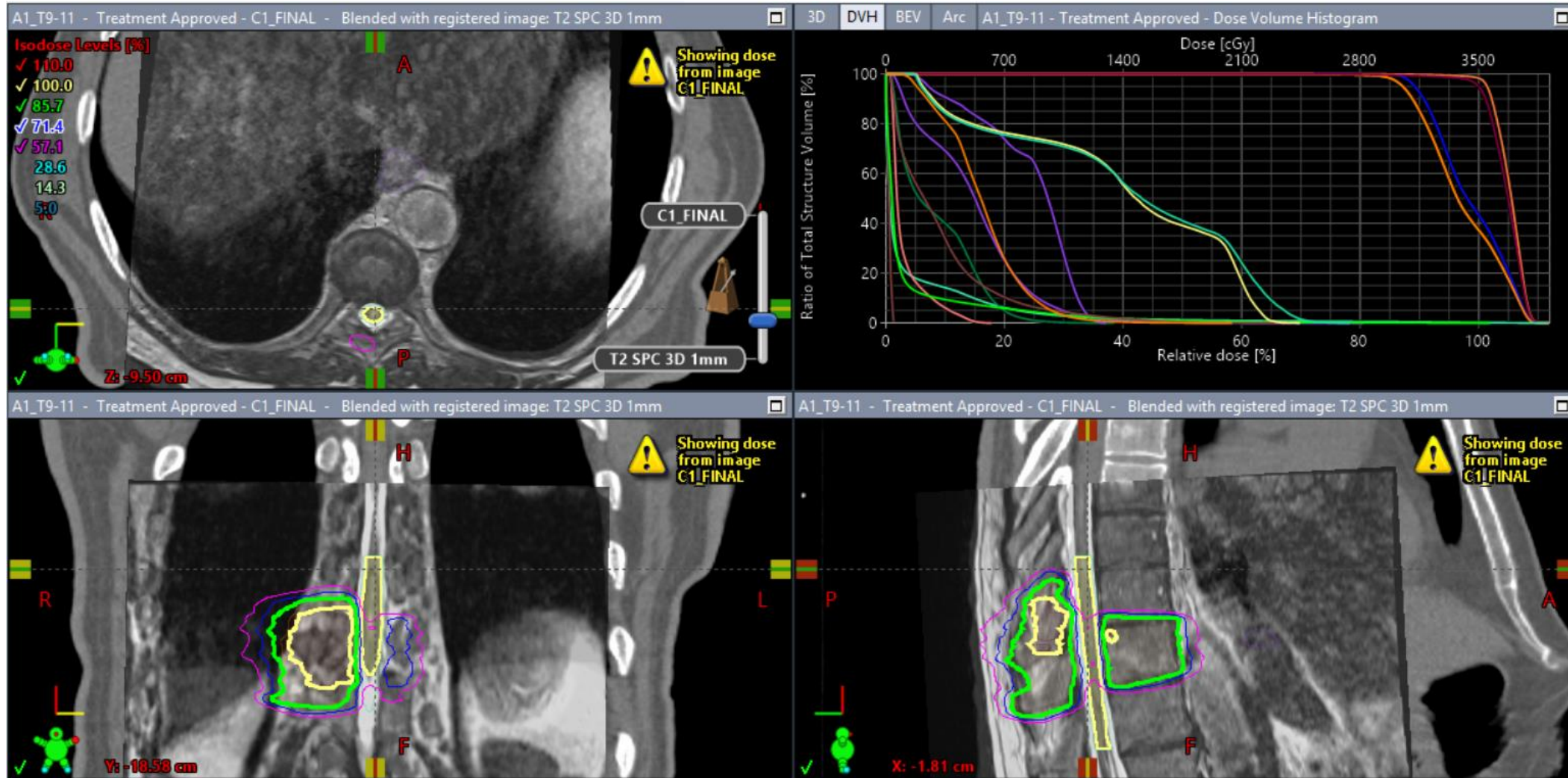
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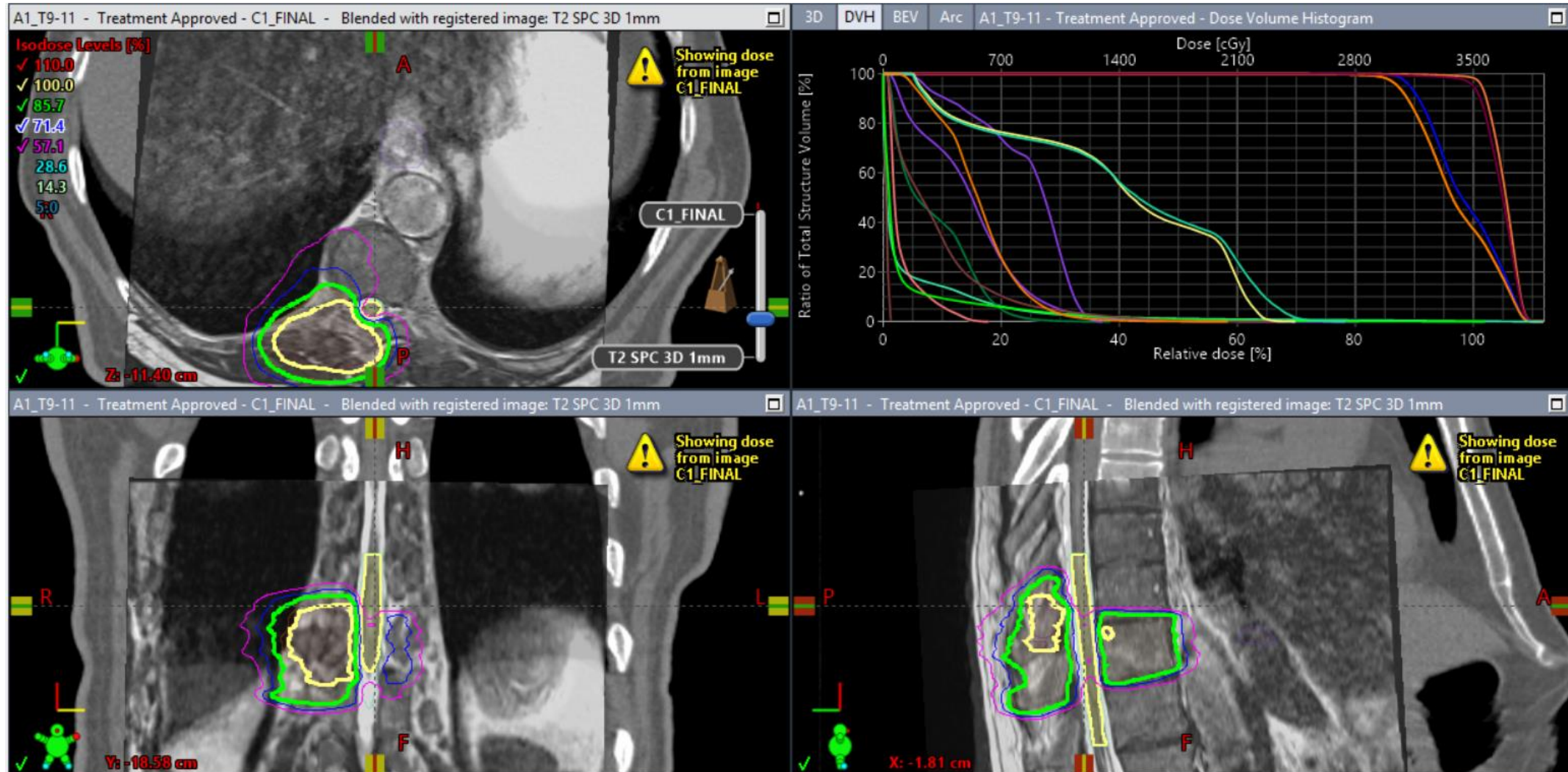
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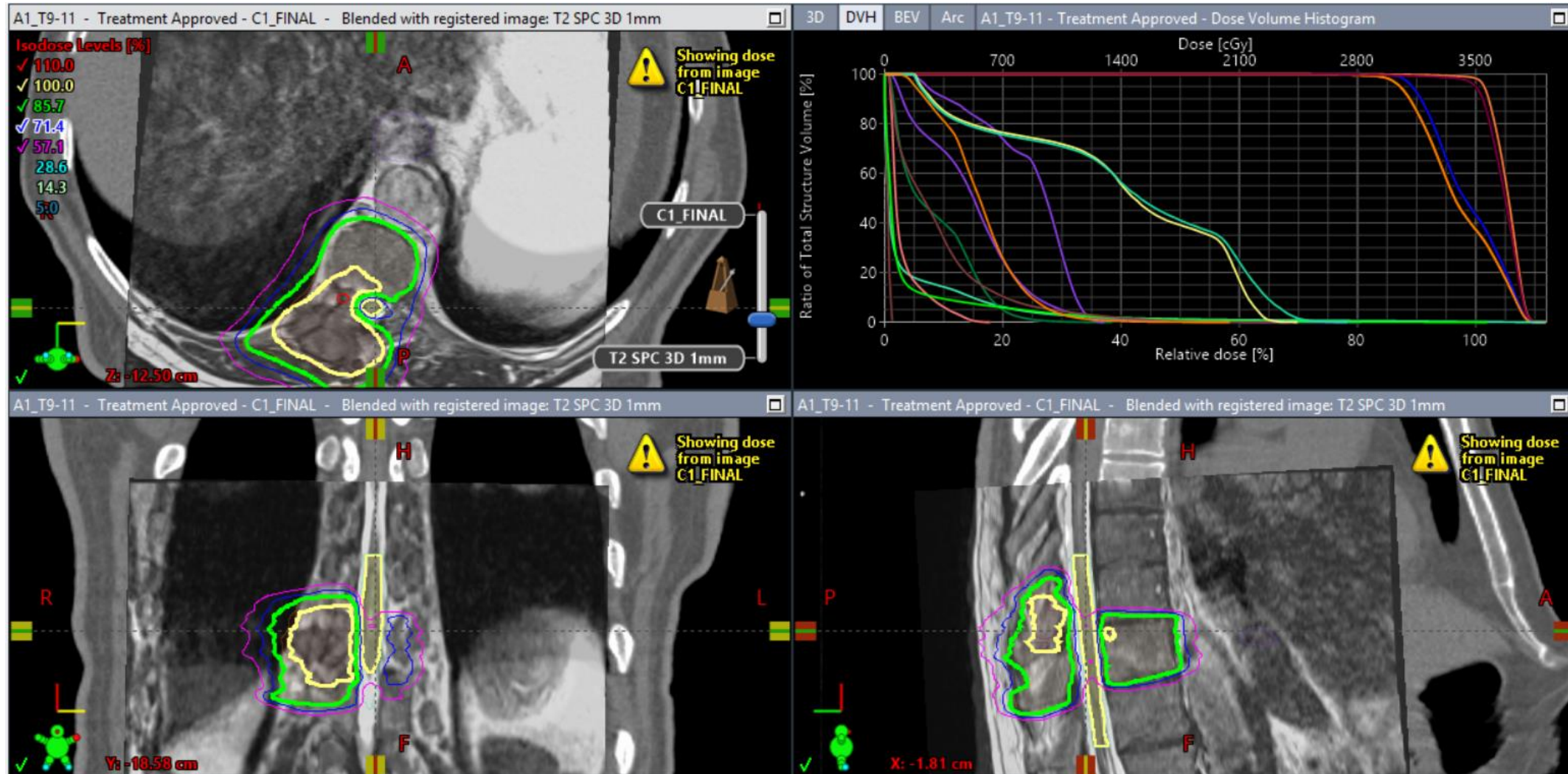
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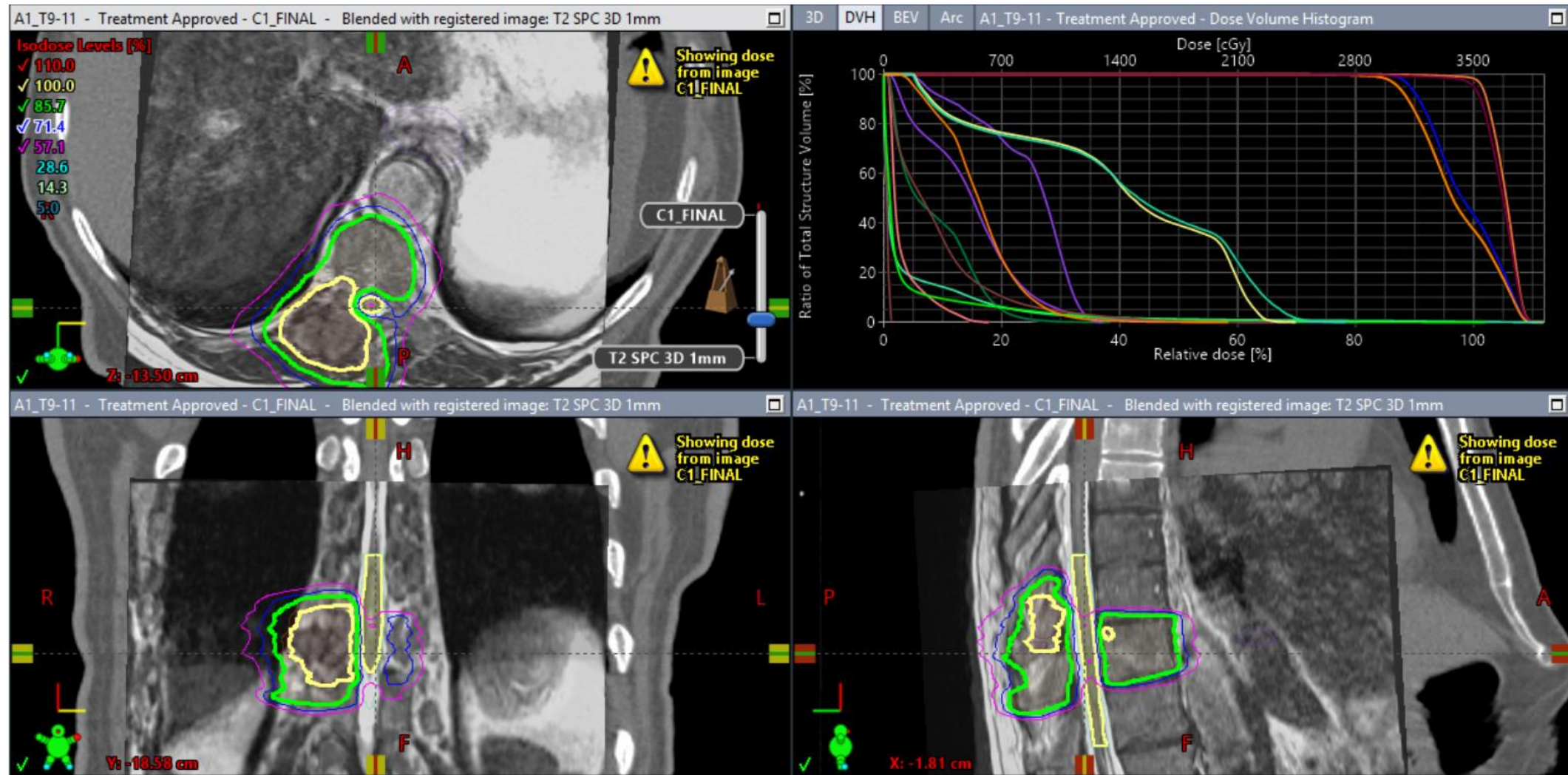
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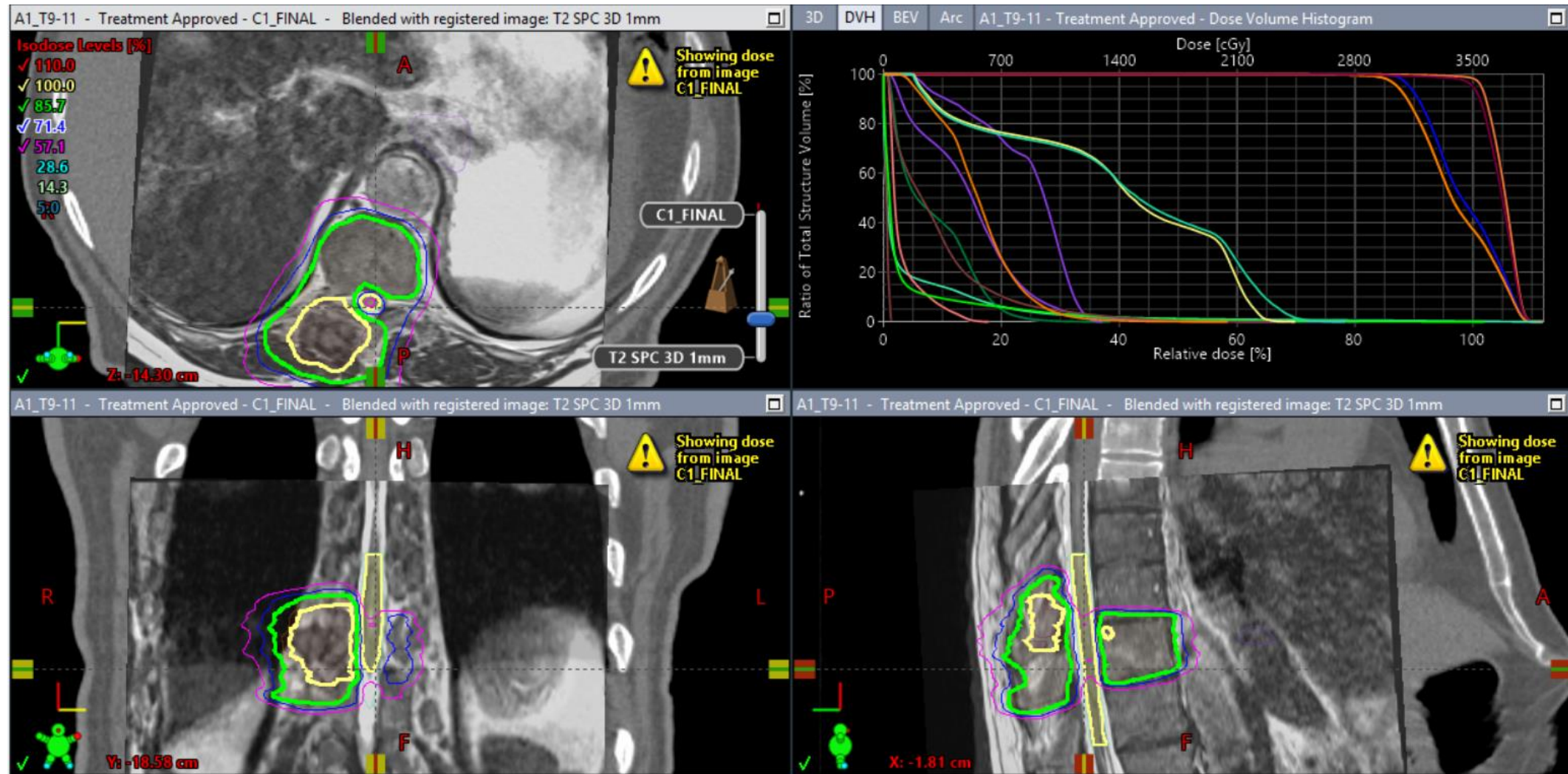
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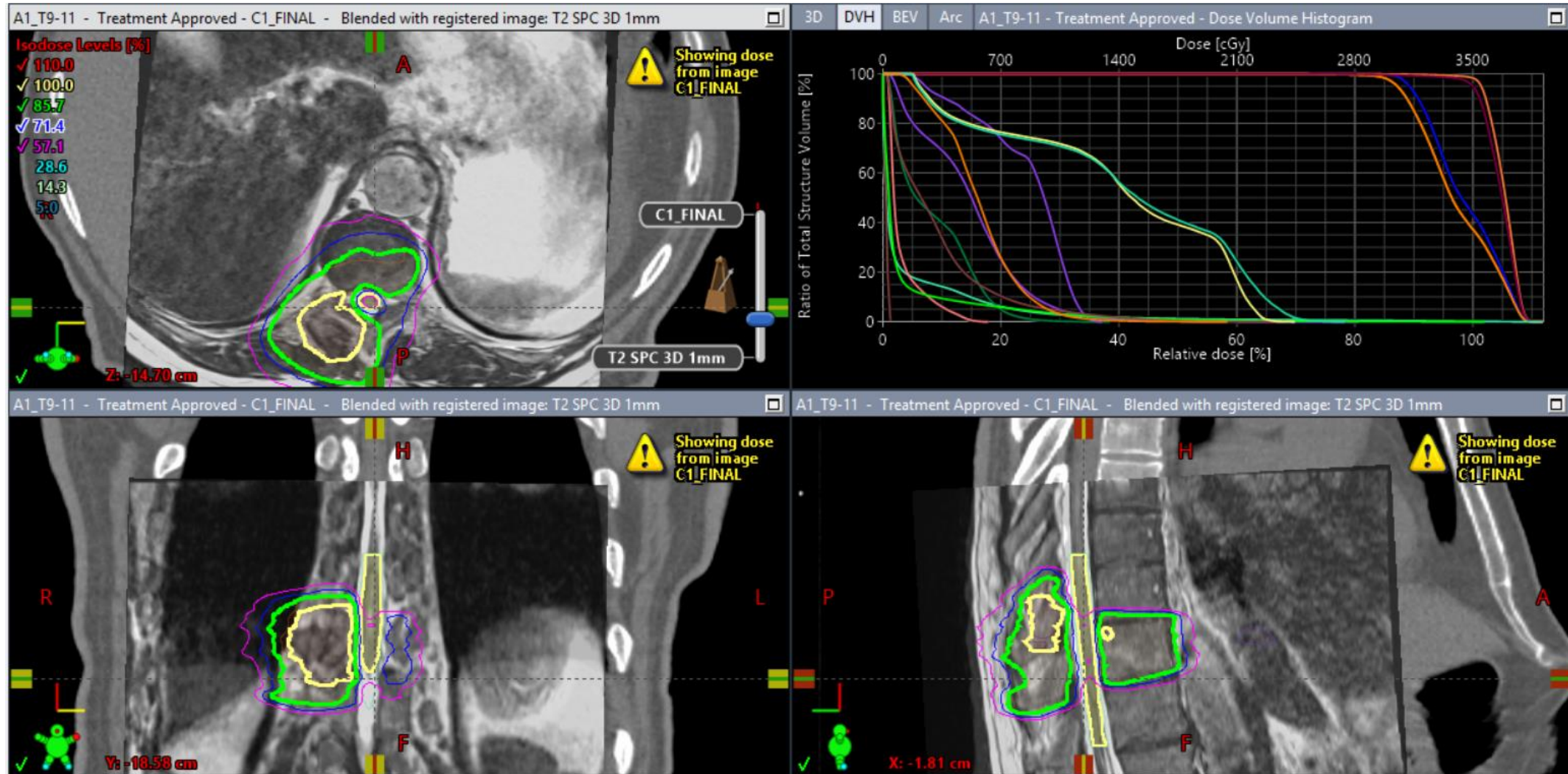
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Question 1 for the audience:

What **DOES NOT** describe stereotactic body radiation therapy?

- a) High dose radiation therapy that is highly conformal to tumor while sparing normal tissues
- b) Daily radiation therapy delivered over multiple weeks (e.g., 20-40 treatments)
- c) Radiation therapy with precision set-up with rigid immobilization and multi-modality imaging
- d) Radiation therapy delivered in 1 to 5 treatments (daily to 2 to 3 times per week)



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2. What are common applications of SBRT in the treatment of cancers?

1. Definitive cancer treatment settings include:
 - Inoperable early stage lung cancer
 - Operable early stage lung cancer
 - Localized prostate cancer
2. Management of oligometastatic disease (goal cure/durable control)
3. Management of metastatic tumors causing symptoms
4. Management of recurrent cancer after prior radiation therapy (to make re-irradiation safely deliverable)



SBRT Definitive Data: Inoperable Early Stage Lung Cancer

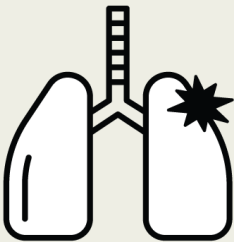
JAMA Oncology

Swaminath et al. LUSTRE Phase 3 Randomized Clinical Trial

RCT: Stereotactic vs Hypofractionated Radiotherapy for Inoperable Stage I Non-Small Cell Lung Cancer

POPULATION

119 Males, 114 Females



Adults with medically inoperable stage I non-small cell lung cancer
Mean age, 75.4 y

INTERVENTION

233 Participants randomized

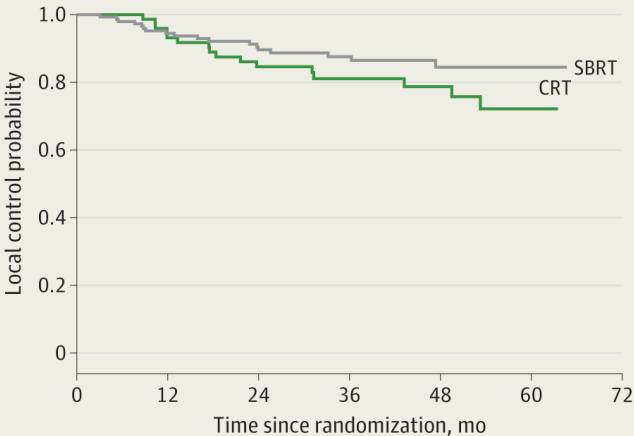


154 Stereotactic body radiation therapy (SBRT)
SBRT of 48 Gy in 4 fractions (peripheral cancers) or 60 Gy in 8 fractions (central cancers)

79 Hypofractionated conventional radiotherapy (CRT)
CRT of 60 Gy in 15 fractions

FINDINGS

Local control was not significantly different between the 2 groups



SETTINGS / LOCATIONS



16 Canadian institutions

PRIMARY OUTCOME

Local control was defined by either local tumor failure or marginal failure. Patients were censored at loss to follow-up or death.

3-y Local control:

SBRT, 87.6%

CRT, 81.2%

Hazard ratio, 0.61; 95% CI, 0.31-1.20; $P = .15$

Swaminath A, Parpia S, Wierzbicki M, et al. Stereotactic vs hypofractionated radiotherapy for inoperable stage I non-small cell lung cancer: the LUSTRE phase 3 randomized clinical trial. *JAMA Oncol*. Published online September 19, 2024. doi:10.1001/jamaoncol.2024.3089

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SBRT Definitive Data: Inoperable Early Stage Lung Cancer

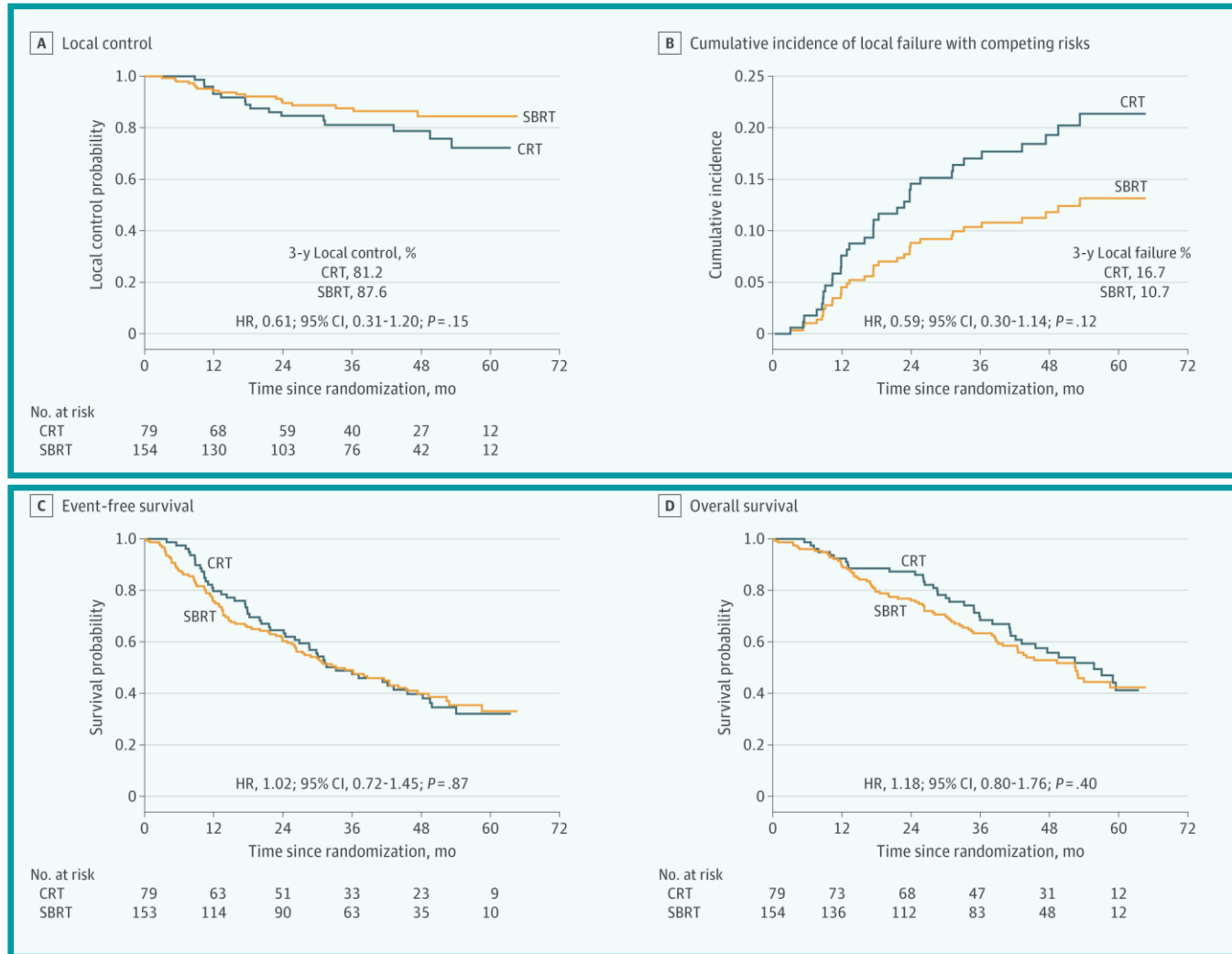


Table. Worst Toxic Effects By Grade and Tumor Location

Toxic effect	No. (%)	
	SBRT	CRT
Worst grade		
Total, No.	154	79
Acute toxic effects (≤ 3 mo)		
Grade 1	41 (27)	21 (27)
Grade 2	11 (7)	4 (5)
Grade 3	1 (<1)	1 (1)
Long-term toxic effects (>3-36 mo)		
Grade 1	39 (25)	17 (22)
Grade 2	21 (14)	10 (13)
Grade 3	7 (5)	1 (1)
Grade 4	0	1 (1)
Grade 5	1 (<1)	0
Grade 3-5 peripheral tumors only		
Total, No.	109	60
Long-term toxic effects (>3-36 mo)		
Grade 3	2 (2)	1 (2)
Grade 4	0	0
Grade 5	0	0
Grade 3-5 central tumors only		
Total, No.	45	19
Long-term toxic effects (>3-36 mo)		
Grade 3	5 (11)	0
Grade 4	0	1 (5)
Grade 5	1 (2)	0

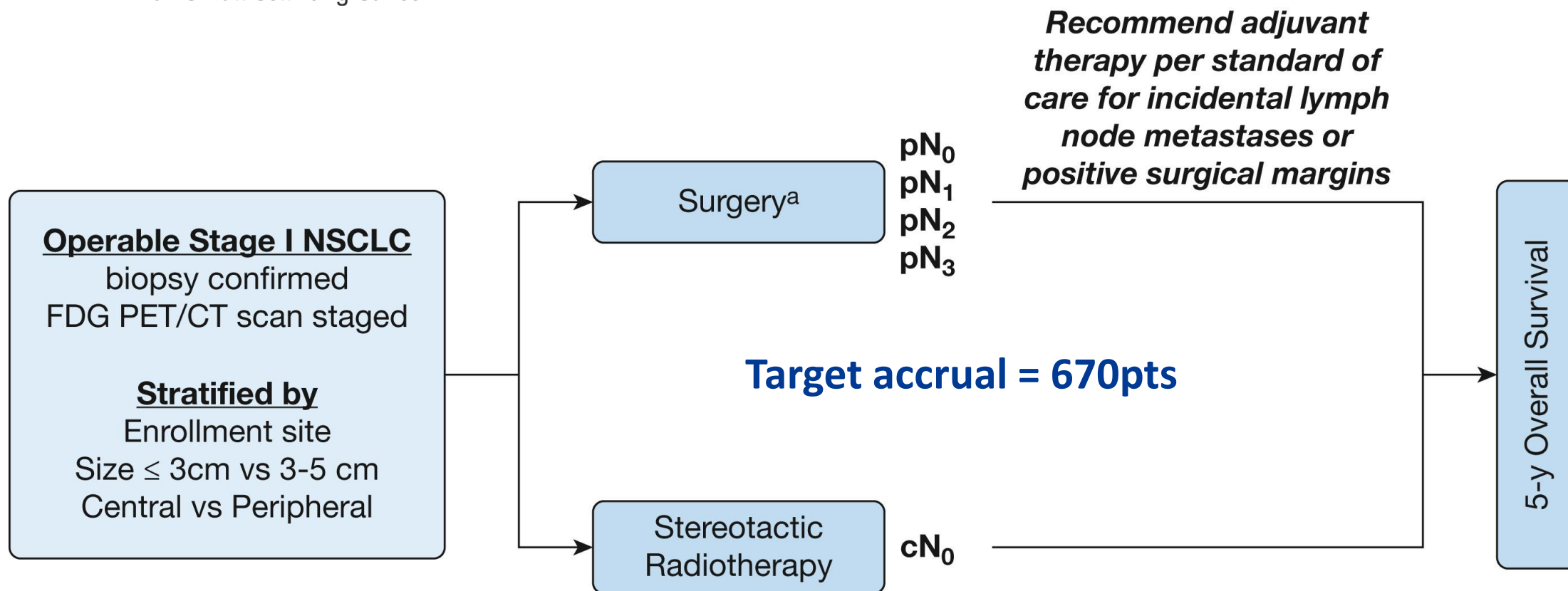
Abbreviations: CRT, hypofractionated conventional radiotherapy; SBRT, stereotactic body radiotherapy.



SBRT Definitive Data: Operable Early Stage Lung Cancer

Protocol for the Veterans Affairs Cooperative Studies Program Study Number 2005

A Phase 3 Randomized Trial of Lung Cancer Surgery or Stereotactic Radiotherapy for Operable Early-Stage
Non-Small Cell Lung Cancer



The NEW ENGLAND JOURNAL of MEDICINE

Stereotactic Body Radiotherapy and Localized Prostate Cancer

A PLAIN LANGUAGE SUMMARY

Based on the NEJM publication: Phase 3 Trial of Stereotactic Body Radiotherapy in Localized Prostate Cancer by N. van As et al. (published October 17, 2024)

In this trial, researchers assessed whether stereotactic body radiotherapy (SBRT) would be noninferior to conventionally or moderately hypofractionated radiotherapy in patients with localized prostate cancer.

Nearly 1.5 million men receive a diagnosis of prostate cancer every year, and a substantial proportion have low- or intermediate-risk disease that can be effectively treated with radiotherapy.

WHY WAS THE TRIAL DONE?

Moderately hypofractionated radiotherapy (i.e., therapy delivered at higher doses over fewer sessions) has been shown to be noninferior to conventionally fractionated radiotherapy. SBRT allows ultrahypofractionated radiotherapy to be delivered with precision, but whether it is as effective as conventionally or moderately hypofractionated radiotherapy at preventing recurrence is uncertain.

Localized Prostate Cancer



HOW WAS THE TRIAL CONDUCTED?

874 men with low- or intermediate-risk localized prostate cancer that did not warrant hormone therapy were randomly assigned to receive SBRT or control radiotherapy. The primary end point was freedom from biochemical failure (increases in prostate-specific antigen [PSA] levels, androgen-deprivation therapy, or orchiectomy) or clinical failure (local or nodal recurrence, distant metastases, or death from prostate cancer).

SBRT
Stereotactic body radiotherapy



433 Patients

CRT
Control radiotherapy



441 Patients

PATIENTS



WHO 874 men
Median age: 69.8 years
Life expectancy: more than 5 years

CLINICAL STATUS Stage T1 or T2, histologically confirmed prostate adenocarcinoma

World Health Organization performance-status score: 0–2 (scale, 0–5; higher scores indicate greater disability)

Low- or intermediate-risk cancer according to National Comprehensive Cancer Network criteria

TRIAL DESIGN

- PHASE 3
- INTERNATIONAL
- OPEN-LABEL
- RANDOMIZED
- CONTROLLED
- LOCATION: 38 CENTERS IN CANADA, IRELAND, AND THE UNITED KINGDOM

The NEW ENGLAND JOURNAL of MEDICINE

RESULTS

SBRT was noninferior to control radiotherapy in achieving freedom from biochemical or clinical failure at 5 years.

The SBRT group had a significantly higher cumulative incidence of late Radiation Therapy Oncology Group (RTOG) grade 2 or higher genitourinary toxic effects than the control radiotherapy group during the 5-year follow-up period (27% vs. 18%). The cumulative incidence of late RTOG grade 2 or higher gastrointestinal toxic effects was similar in the two groups.

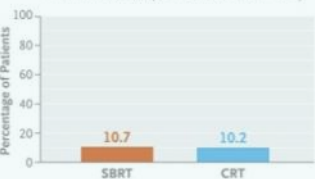
Freedom from Biochemical or Clinical Failure

Unadjusted hazard ratio for failure, 0.73 (90% CI, 0.48–1.12; P=0.004 for noninferiority)



Gastrointestinal Toxic Effects

Hazard ratio, 1.03 (95% CI, 0.68–1.56; P=0.94)



TREATMENT DURATION



SBRT (36.25 Gy in 5 fractions) was administered over a period of only 1 or 2 weeks, whereas control radiotherapy (62 Gy in 20 fractions or 78 Gy in 39 fractions) was administered over a period of 4 or 7.5 weeks.

LIMITATIONS AND REMAINING QUESTIONS

- 87% of the patients in the trial were White, which limits the generalizability of the findings.
- The proportion of the patients from this trial who would now receive active surveillance rather than treatment is unclear, given the lack of data showing that treatment influences overall survival among some patients with localized disease.
- Results of this trial are not applicable to men with higher-risk disease. A companion trial in this population is under way.

CONCLUSIONS

In patients with low- or intermediate-risk, localized prostate cancer, SBRT was noninferior to conventionally or moderately hypofractionated regimens in achieving freedom from biochemical or clinical failure.

LINKS: FULL ARTICLE | NEJM QUICK TAKE

FURTHER INFORMATION

Trial registration: ClinicalTrials.gov number, NCT01584258

Trial funding: Accuray and others

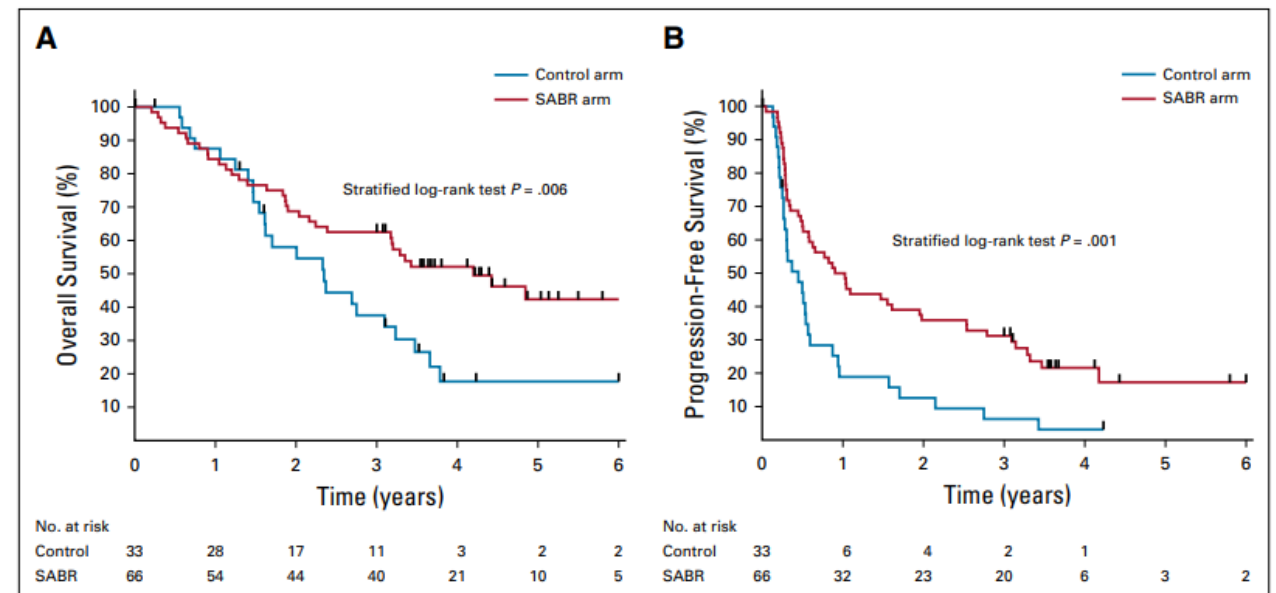
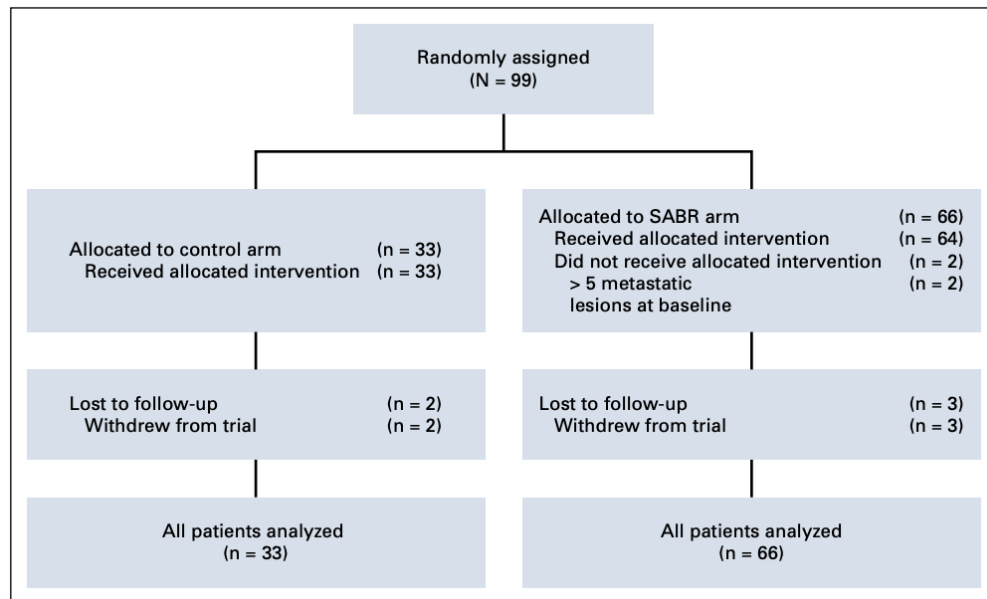
Full citation: van As N, Griffin C, Tree A, et al. Phase 3 trial of stereotactic body radiotherapy in localized prostate cancer. N Engl J Med 2024;391:1413-25. DOI: 10.1056/NEJMoa2403365

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SBRT Oligometastatic Cancers: SBRT to 1-5 metastases

Stereotactic Ablative Radiotherapy for the Comprehensive Treatment of Oligometastatic Cancers: Long-Term Results of the SABR-COMET Phase II Randomized Trial

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal



SBRT Oligoprogressive Cancer: SBRT 1-5 oligoprogressive mets

Consolidative Use of Radiotherapy to Block (CURB) Oligoprogression - Randomised Study of Standard-of-Care Systemic Therapy with or without Stereotactic Body Radiotherapy in Patients with Oligoprogressive Cancers of the Breast and Lung. Tsai et al. The Lancet 2025

THE LANCET

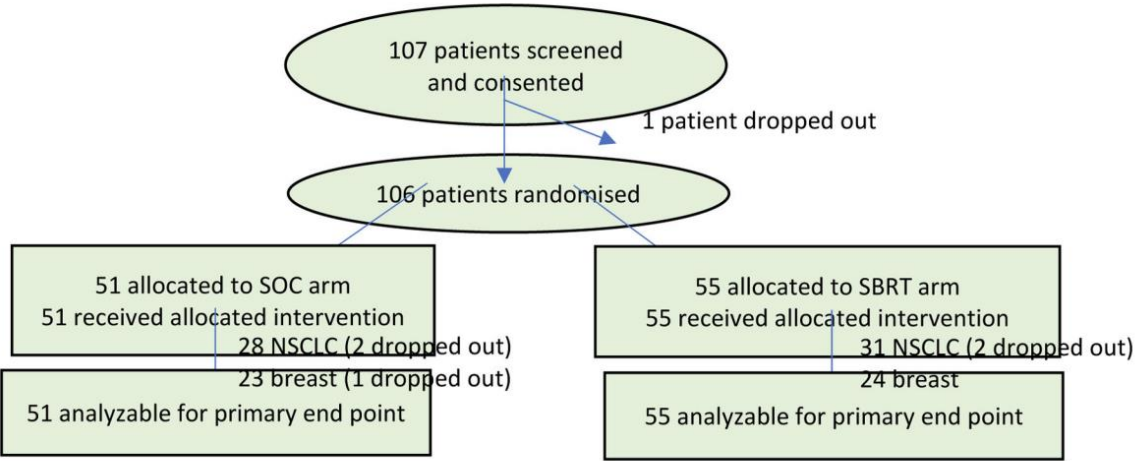


Figure 1. CONSORT Diagram. Illustration of patients enrolled on study and arm assignment

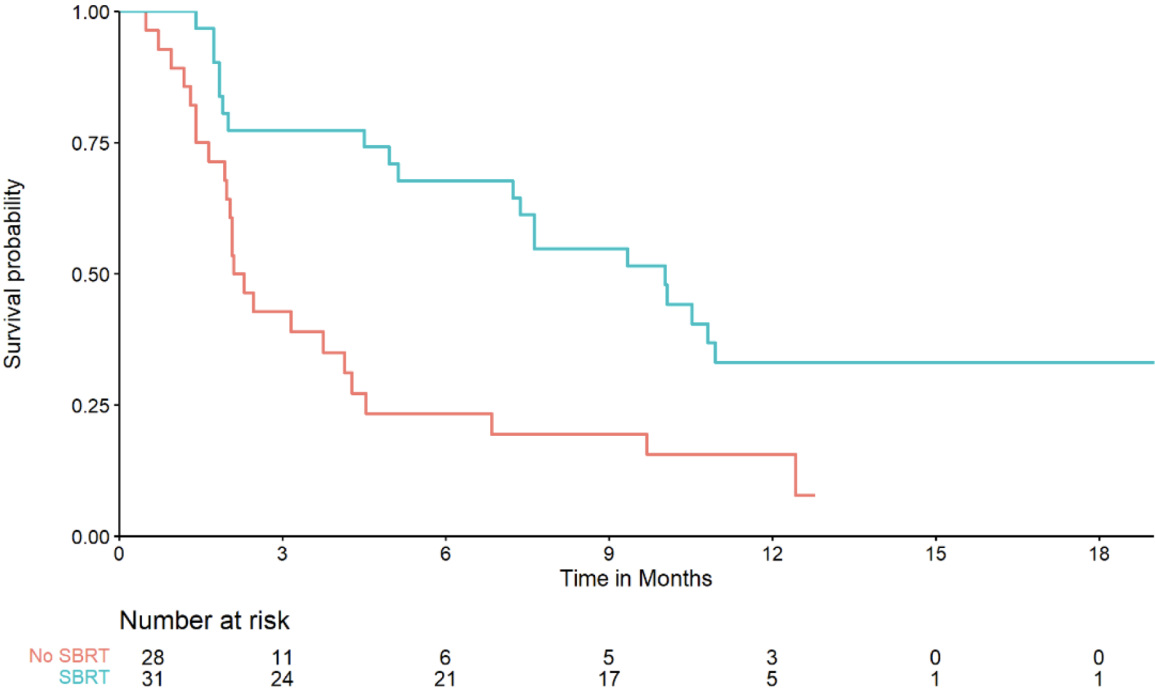
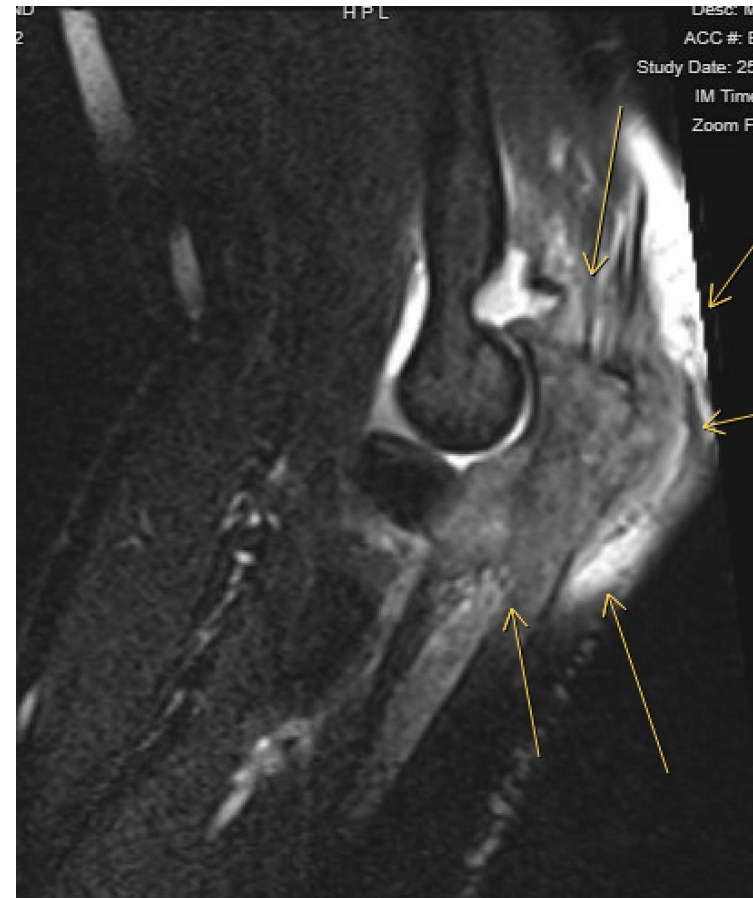
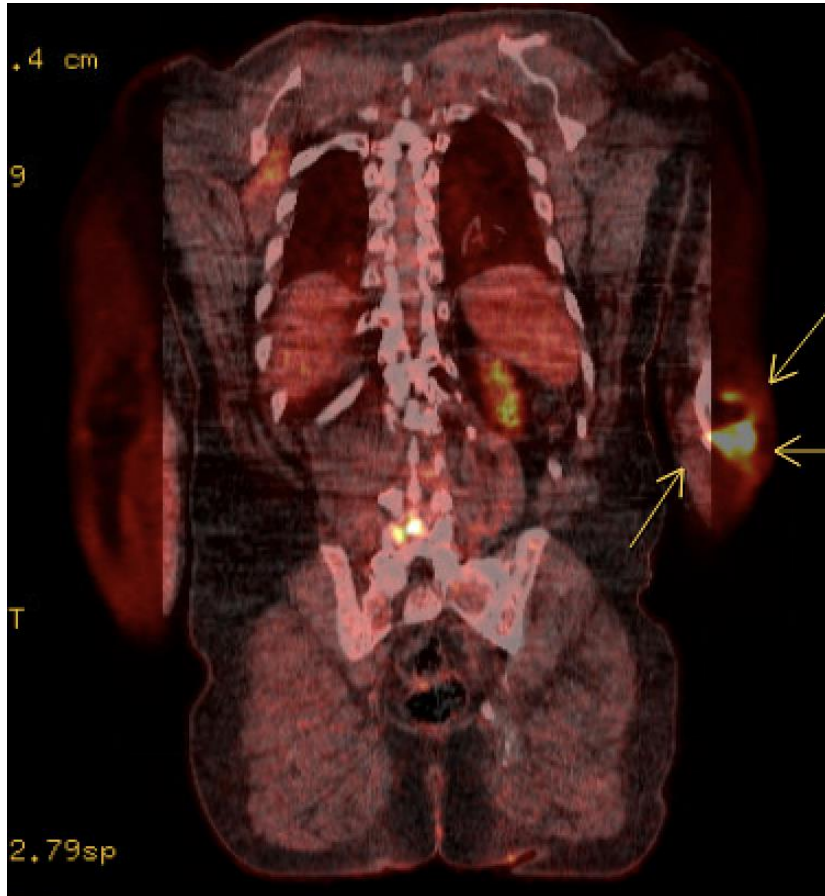


Figure 2. Progression Free Survival. A.) Median PFS in the entire cohort was increased in the SBRT arm vs. No SBRT arm (7.2 vs 3.2 months, stratified log-rank p=0.003). B.) Median PFS was not different in patients with breast cancer in each arm (4.2 vs. 4.4 months; stratified log-rank p=0.2). C.) Median PFS increased 4-fold in patients with NSCLC treated with SBRT (10 vs. 2.2 months, stratified log-rank p=0.004). SBRT: stereotactic body radiotherapy



SBRT for Symptomatic Metastases

- 65 yo M, ECOG 1, met colon cancer x 4 years, bone/lung mets, stable on systemic tx
- Single, progressive, painful site in the left elbow, pain 5/10, unable to work
- Referred to radiation oncology, discussed with orthopedics – no surgical option.

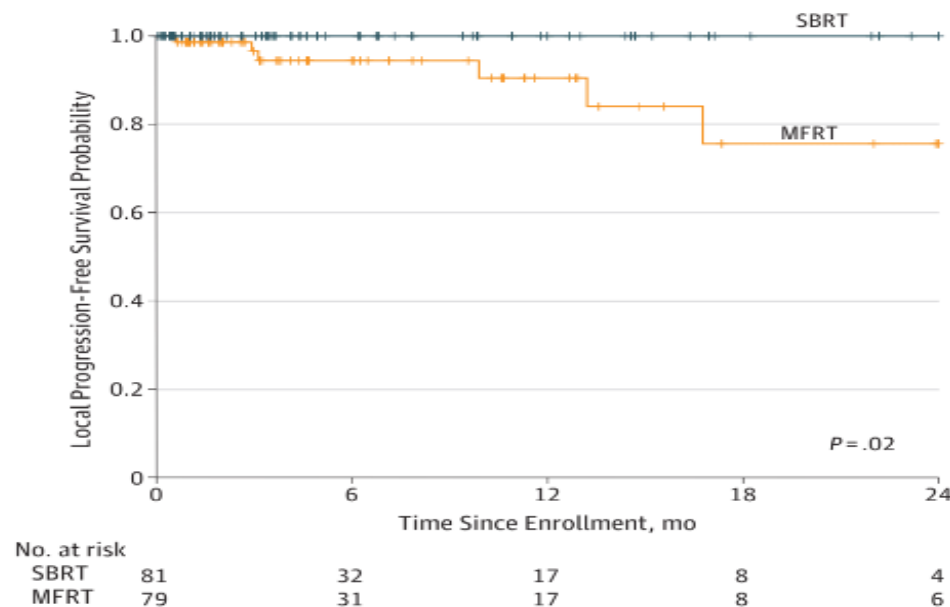


SBRT for Symptomatic Metastases

Nguyen et al. *JAMA Oncology* 2019: Single institution, phase II RCT, non-inferiority study of 160 pts with painful non-spine bone mets randomized to SBRT (12-16Gy SF) vs. MFRT (30Gy in 10fx); Primary endpoint pain response

- Pain Response(CR+PR) SBRT>MFRT:
 - 2 weeks (62% vs. 36%, p=0.01)
 - 3 months (72% vs. 49%, p=0.03)
 - 9 months (77% vs. 46%, p=0.03)
- Local Control SBRT>MFRT
 - 1 year (100% vs. 90.5%, p=0.01)
 - 2 years (100% vs. 75.6%, p=0.01)

Figure 2. Local Progression-Free Survival According to Treatment



MFRT indicates standard-dose multifraction radiation therapy (10 fractions of 3 Gy each, for a total of 30 Gy); SBRT, high-dose, single-fraction stereotactic radiation therapy with a dose of 12 Gy or 16 Gy (solid line).



SBRT for Symptomatic Metastases

Sahgal et al. *Lancet Oncology* 2021;

CCTG.SC24 Phase 2-3 RCT

(Canada/Australia)

- 229 painful bone mets pts randomized to 24Gy/2fx SBRT vs. 20Gy/5fx conventional RT
- Primary endpoint complete pain response at 3 months

	Conventional external beam radiotherapy group (n=115)	Stereotactic body radiotherapy group (n=114)	p value
1-month assessment			
Complete response	20 (17%)	30 (26%)	0.10*
Partial response	33 (29%)	34 (30%)	..
Stable pain	38 (33%)	26 (23%)	..
Progressive pain	14 (12%)	9 (8%)	..
Indeterminant	10 (9%)	15 (13%)	..
Mean daily OME consumption, mg	44 (122)	27 (95)	0.26
3-month assessment			
Complete response	16 (14%)	40 (35%)	0.0002*
Partial response	29 (25%)	20 (18%)	..
Stable pain	34 (30%)	27 (24%)	..
Progressive pain	14 (12%)	7 (6%)	..
Indeterminant	22 (19%)	20 (18%)	..
Mean daily OME consumption, mg	43 (106)	37 (97)	0.70
Mean change in SINS from baseline	-0.49 (1.61)	-0.94 (1.69)	0.034
6-month assessment			
Complete response	18 (16%)	37 (32%)	0.0036*
Partial response	18 (16%)	10 (9%)	..
Stable pain	32 (28%)	26 (23%)	..
Progressive pain	8 (7%)	5 (4%)	..
Indeterminant	39 (34%)	36 (32%)	..
Mean daily OME consumption, mg	36 (126)	36 (84)	1.00
Mean change in SINS from baseline	-0.74 (1.99)	-0.73 (1.86)	0.88



SBRT for Symptomatic Metastases

Zeng et al. *IJROBP* 2022; CCTG.SC24 Phase 2-3 RCT (Canada/Australia) of 229 painful bone mets pts randomized to 24Gy/2fx SBRT vs. 20Gy/5fx conventional RT

Local Control at Site (by MRI) SBRT vs. cEBRT:

- 6 months: 2.8%(95% CI, 0.8%-7.4%) vs 11.2% (95% CI, 6.9%-16.6%)
- 12 months 6.1% (95% CI, 2.5%-12.1%) vs 28.4% (95% CI, 21.3%-35.9%),and
- 24 months: 14.8% (95% CI, 8.2-23.1%) vs 35.6% (95% CI, 27.8%-43.6%), respectively (P<.001)

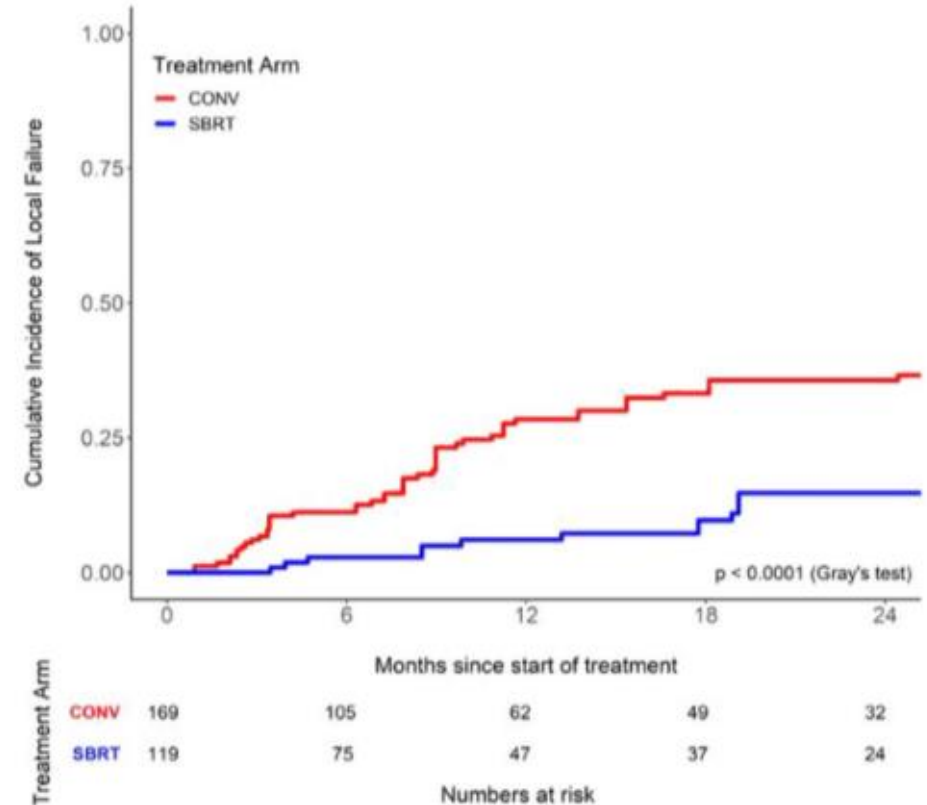
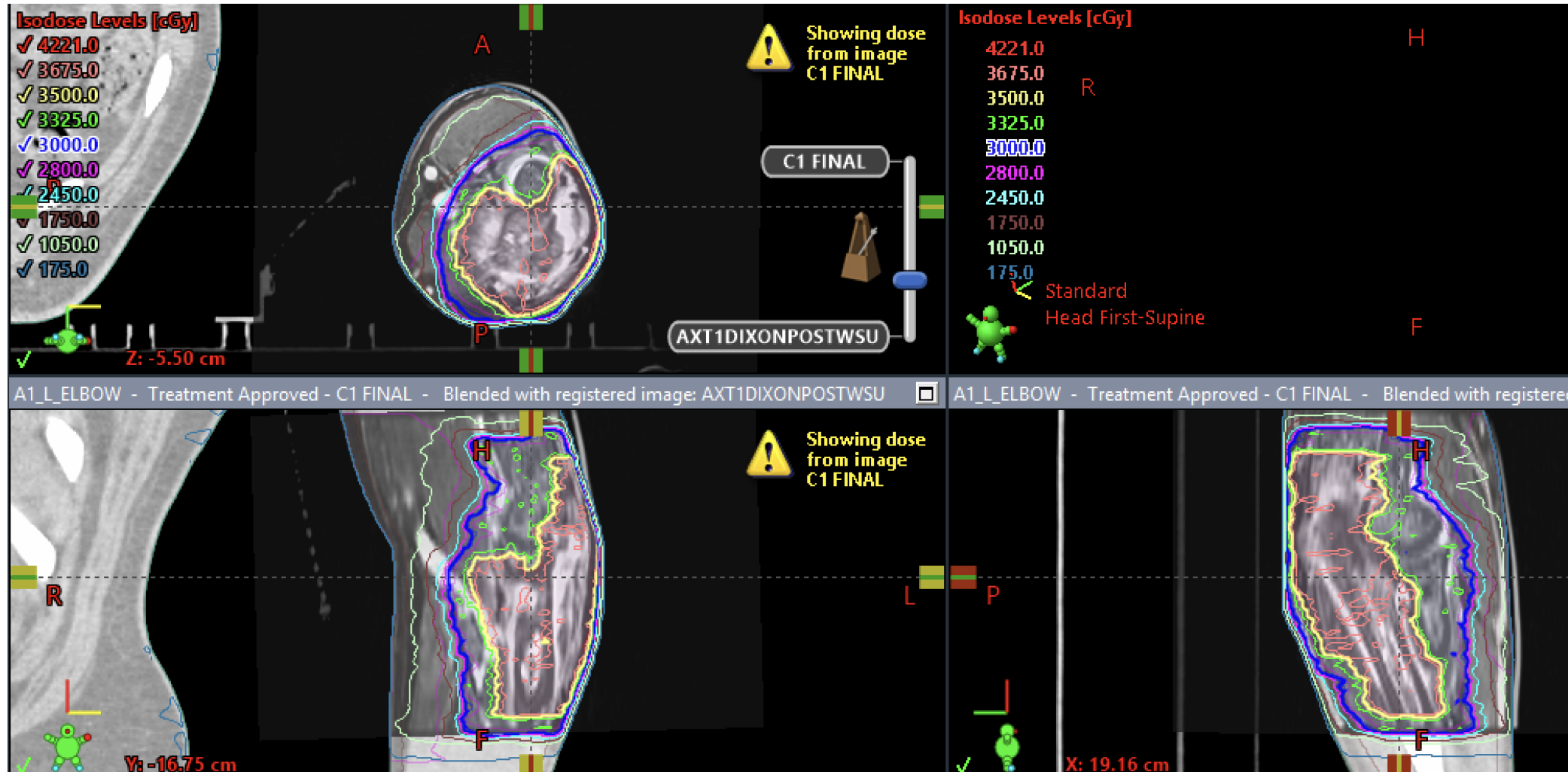


Fig. 1. Cumulative incidence of local failure in the stereotactic body radiation therapy (SBRT) and conventional external beam radiation therapy (cEBRT) cohorts demonstrating statistically significant increase in risk of local failure in the latter. Abbreviation: CCTG = Canadian Cancer Trials Group.



65 yo M, ECOG 1, metastatic colon cancer x 4 years, bone and lung metastases, stable on currently systemic therapy except for single progressive, painful site in the left elbow, pain 5/10, unable to work at construction job → SBRT 35Gy in 5fx to L elbow March 2024, at 3mo FU had complete pain response (0/10) and is back to work.



Question 2 for the audience:

What are the applications for stereotactic body radiation therapy supported by randomized trials?

- a) Curative management of early/intermediate risk prostate cancer and inoperable early stage lung cancer
- b) Management of oligometastatic/oligoprogressive disease to prolong progression free and overall survival
- c) Management of metastases causing symptoms
- d) All of the above



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TAKE HOME MESSAGES

1. SBRT is a novel, precision application of advanced imaging and radiation therapy delivery techniques that allows the delivery of ablative doses of radiation therapy to tumors with minimal dose to surrounding normal tissues
2. SBRT has applications in the curative management of primary malignancies, such as early stage lung cancer and prostate cancer, and in the management of metastatic disease to improve survival outcomes and to reduce symptoms/improve QoL



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