News Briefing: Monday, October 24

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Conventional vs hypofractionated radiotherapy for high-risk prostate cancer: 7-year outcomes of the randomized, non-inferiority, phase 3 PCS5 trial

Tamim M. Niazi, MD, McGill University

Association of prostate-specific antigen screening rates and subsequent metastatic prostate cancer incidence in a national healthcare system

Brent Rose, MD, University of California, San Diego

NRG/RTOG 1112: Randomized phase III study of sorafenib vs. stereotactic body radiation therapy followed by sorafenib in hepatocellular carcinoma

Laura A. Dawson, MD, FASTRO, Princess Margaret Cancer Centre

Examining the impact of direct patient care for medical physicists: A randomized prospective phase III trial

Todd F. Atwood, PhD, University of California, San Diego

FAST-01: Results of the first-in-human study of proton FLASH radiotherapy

Emily C. Daugherty, MD, University of Cincinnati Cancer Center

Featured Experts

- Jeff M. Michalski, MD, MBA, FASTRO, Washington University School of Medicine in St. Louis, Incoming ASTRO President
- Karyn A. Goodman, MD, FASTRO, Icahn School of Medicine at Mount Sinai
- Julianne M. Pollard-Larkin, PhD, The University of Texas MD Anderson Cancer Center

AI & EI: CARING FOR THE PATIENT IN A WIRELESS WORLD

ASTRO ANNUAL 2022 MEETING

Conventional vs. hypofractionated radiotherapy for high-risk prostate cancer:

7-year outcomes of the randomized, non-inferiority, phase 3 PCS5 trial

Abstract 4

Presented by:

Tamim M. Niazi, MD
McGill University

Disclosure & Study Team

- Research/Educational funds: Abbvie, Astellas, Bayer, Janssen, Amgen, Sanofi, Astrazeneca, TerSera
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- This study was supported by funding from Sanofi Canada.

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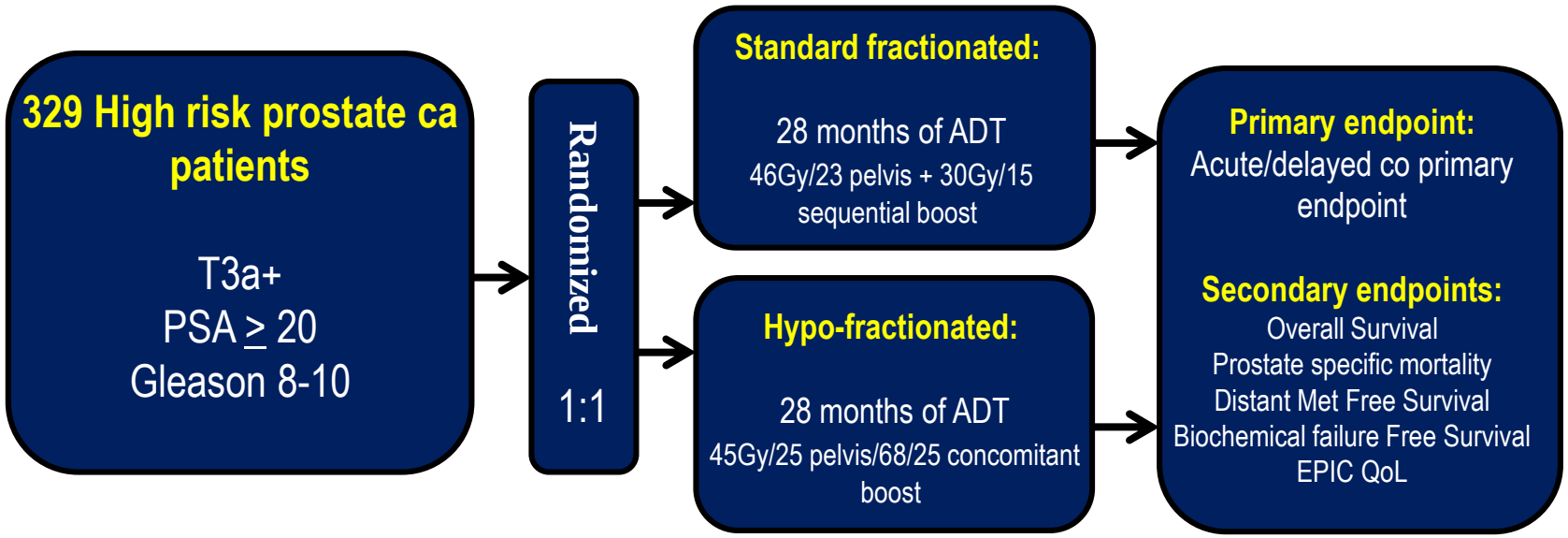
Rationale

- Localized prostate cancer:
  - Low risk
  - Intermediate Risk
  - High risk
- Moderate hypofractionated RT:
  - Predominantly intermediate or mixed risk groups

- Majority of patients with high-risk prostate cancer are still treated with conventional fractionation ~8 weeks.

PCS5 Schema

Multicenter Phase III Canadian trial

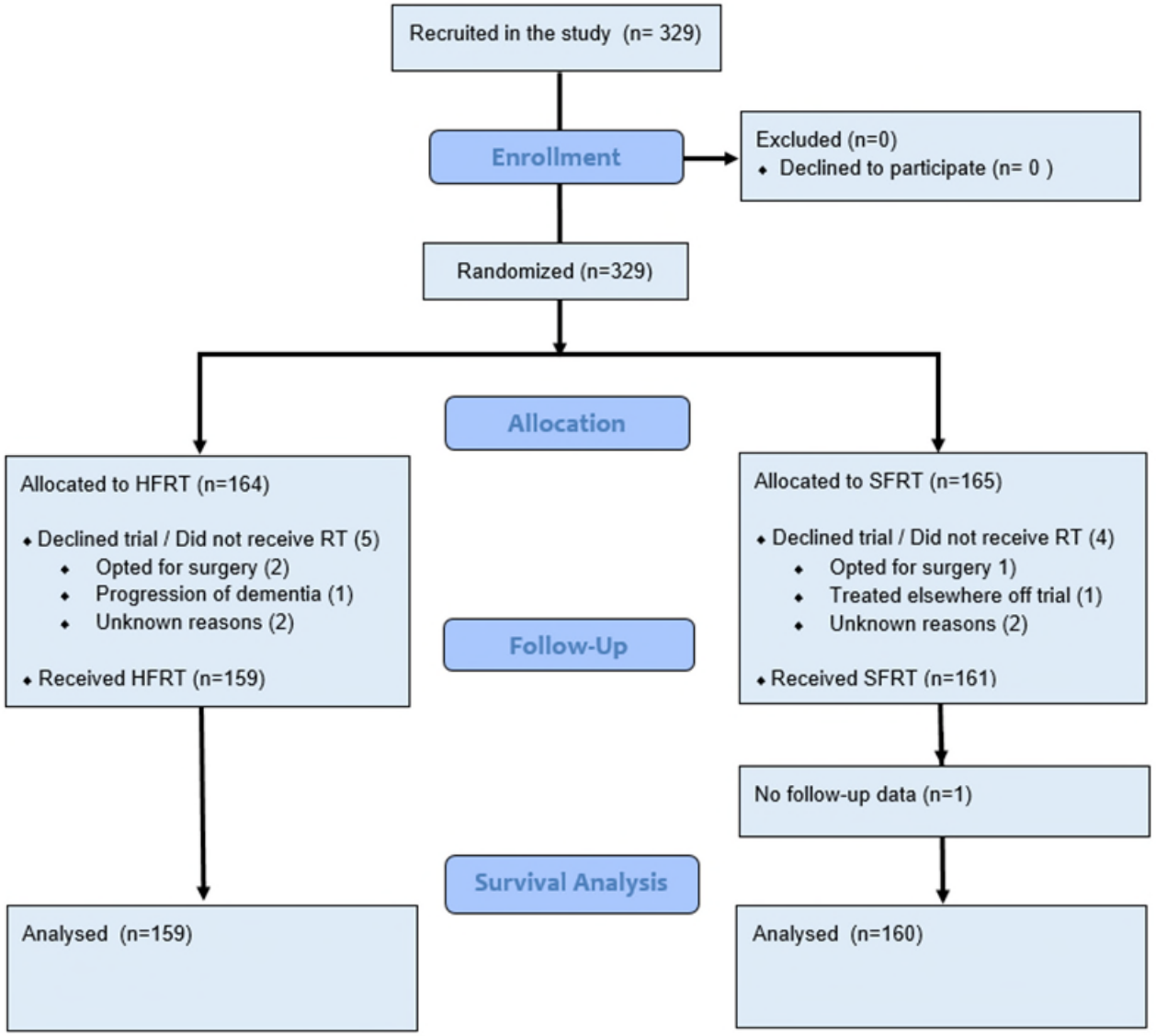


Enrollment: - Feb 2012-Mar 2015
- 12 Canadian sites

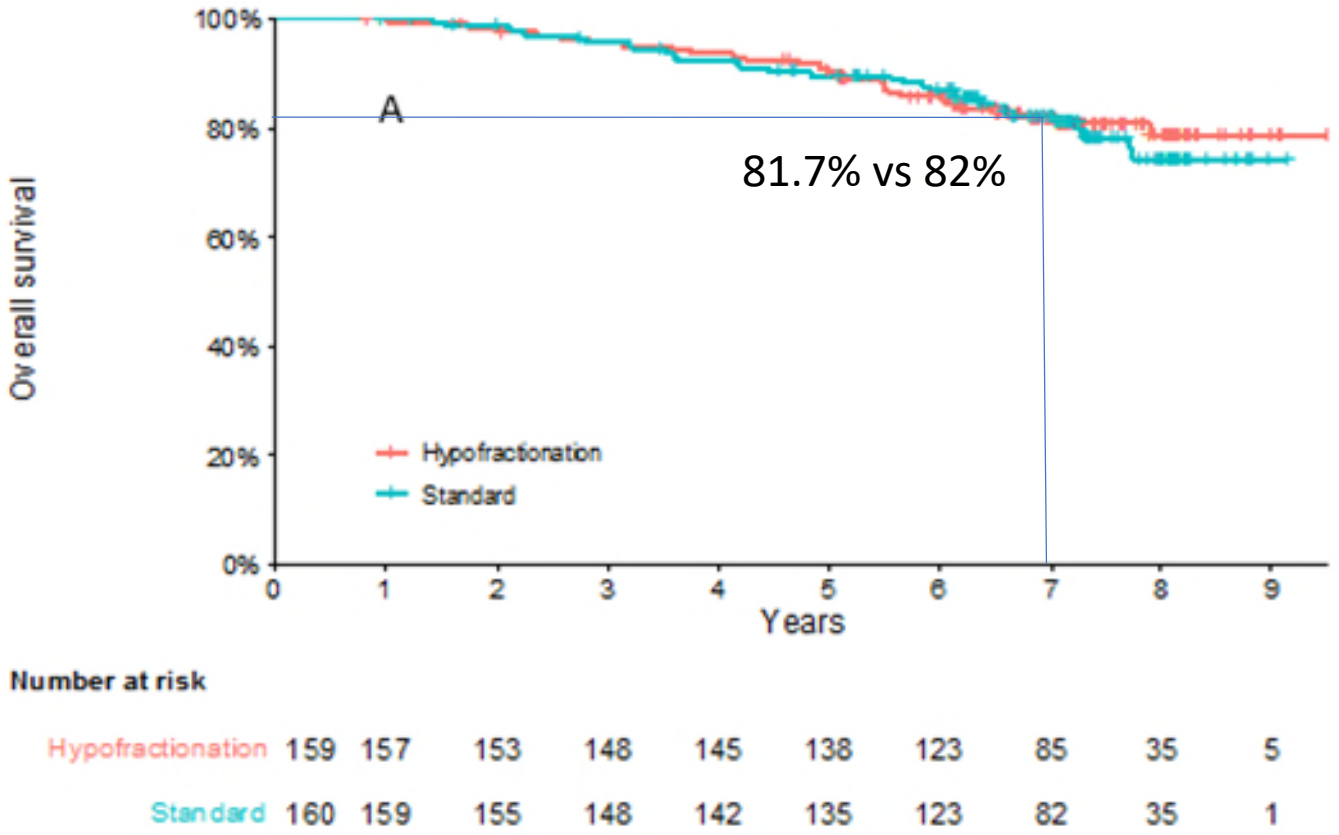
Baseline demographics and disease characteristics

Characteriestic		Entire Cohort	HF arm	SF arm
Total		320	159 (49.7%)	161 (50.3%)
Age				
	Median (IQR)	72 (68-76)	73 (68-76)	72 (68-75)
T stage, n(%)				
	T1	84 (26.3%)	37 (23.3%)	47 (29.2%)
	T2	152 (47.5%)	76 (47.8%)	76 (47.2%)
	T3	81 (25.3%)	45 (28.3%)	36 (22.4%)
	T4	2 (0.6%)	1 (0.6%)	1 (0.6%)
	unknown	1 (0.3%)	0 (0.0%)	1 (0.6%)
PSA				
	Median (IQR)	11.6 (7.0-21.0)	11.7 (5.0-9.0)	11.1 (5.0-9.0)
PSA				
	0-<5	37 (11.6%)	18 (11.3%)	19 (11.8%)
	5-<10	101 (31.6%)	47 (29.6%)	54 (33.5%)
	10-<20	95 (29.7%)	58 (36.5%)	37 (23.0%)
	20-<50	68 (21.3%)	28 (17.6%)	40 (24.8%)
Gleason				
	6	6 (1.9%)	4 (2.5%)	2 (1.2%)
	7	48 (15.0%)	25 (15.7%)	23 (14.2%)
	8	156 (48.8%)	72 (45.3%)	84 (52.2%)
	9	99 (30.9%)	53 (33.3%)	46 (28.6%)
	10	11 (3.4%)	5 (3.1%)	6 (3.7%)
Testosterone				
	Median (range)	11.6 (0.0-34.0)	11.1 (0.0-22.9)	12.0 (0.0-34.0)
	Mean (SD)	11.9 (5.3)	11.1 (4.8)	12.6 (5.6)
	Unknown	9 (2.8%)	4 (2.5%)	5 (3.1%)
IPSS				
	Median (range)	7.0 (0.0-35.0)	8.0 (0.0-35.0)	7.0 (0.0-34.0)
	Mean (SD)	8.8 (6.8)	9.2 (6.6)	8.4 (7.0)
	Unknown	6 (1.9%)	6 (3.8%)	0 (0.0%)
IIEF				
	Median (range)	12.0 (0.0-30.0)	11.0 (1.0-30.0)	12.0 (0.0-25.0)
	Mean (SD)	12.0 (7.6)	12.0 (7.7)	11.9 (7.5)
	Unknown	98 (30.6%)	48 (30.2%)	50 (31.1%)
ED				
	Yes	203 (63.4%)	100 (62.9%)	103 (64.0%)
	No	117 (36.6%)	59 (37.1%)	58 (36.0%)
Technique				
	IMRT	196 (61.3%)	95 (59.7%)	101 (62.7%)
	3DCRT	118 (36.9%)	61 (38.4%)	57 (35.4%)
	Unknown	6 (1.9%)	3 (1.9%)	3 (1.9%)

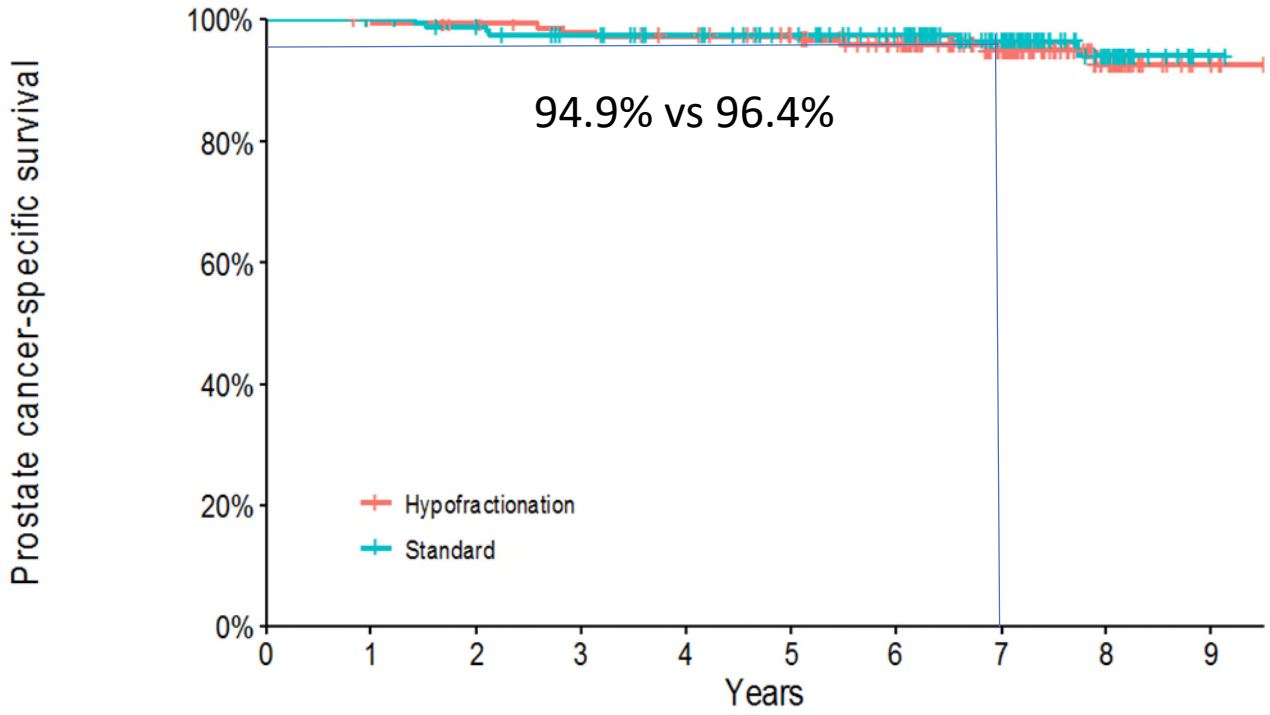
Flowchart:


Recruited in the study (n= 329)
Enrollment
Excluded (n=0)
Declined to participate (n= 0)
Randomized (n=329)
Allocation
Allocated to HFRT (n=164)
Declined trial / Did not receive RT (5)
Opted for surgery (2)
Progression of dementia (1)
Unknown reasons (2)
Received HFRT (n=159)
Allocated to SFRT (n=165)
Declined trial / Did not receive RT (4)
Opted for surgery 1)
Treated elsewhere off trial (1)
Unknown reasons (2)
Received SFRT (n=161)
Follow-Up
No follow-up data (n=1)
Survival Analysis
Analysed (n=159)
Analysed (n=160)

Overall survival by study arm



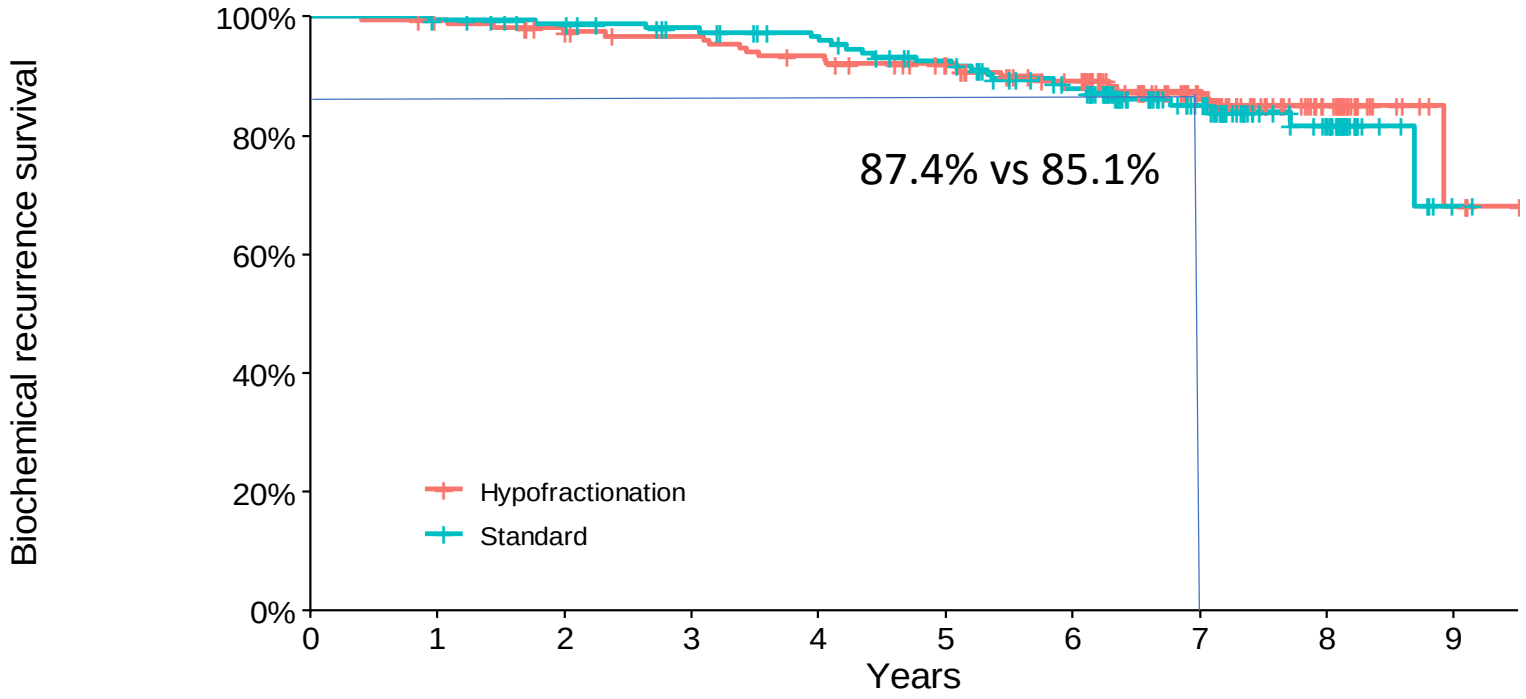
Prostate-specific mortality



Number at risk

Hypofractionation	159	157	153	148	145	138	123	85	35	5
Standard	160	159	155	148	142	135	123	82	35	1

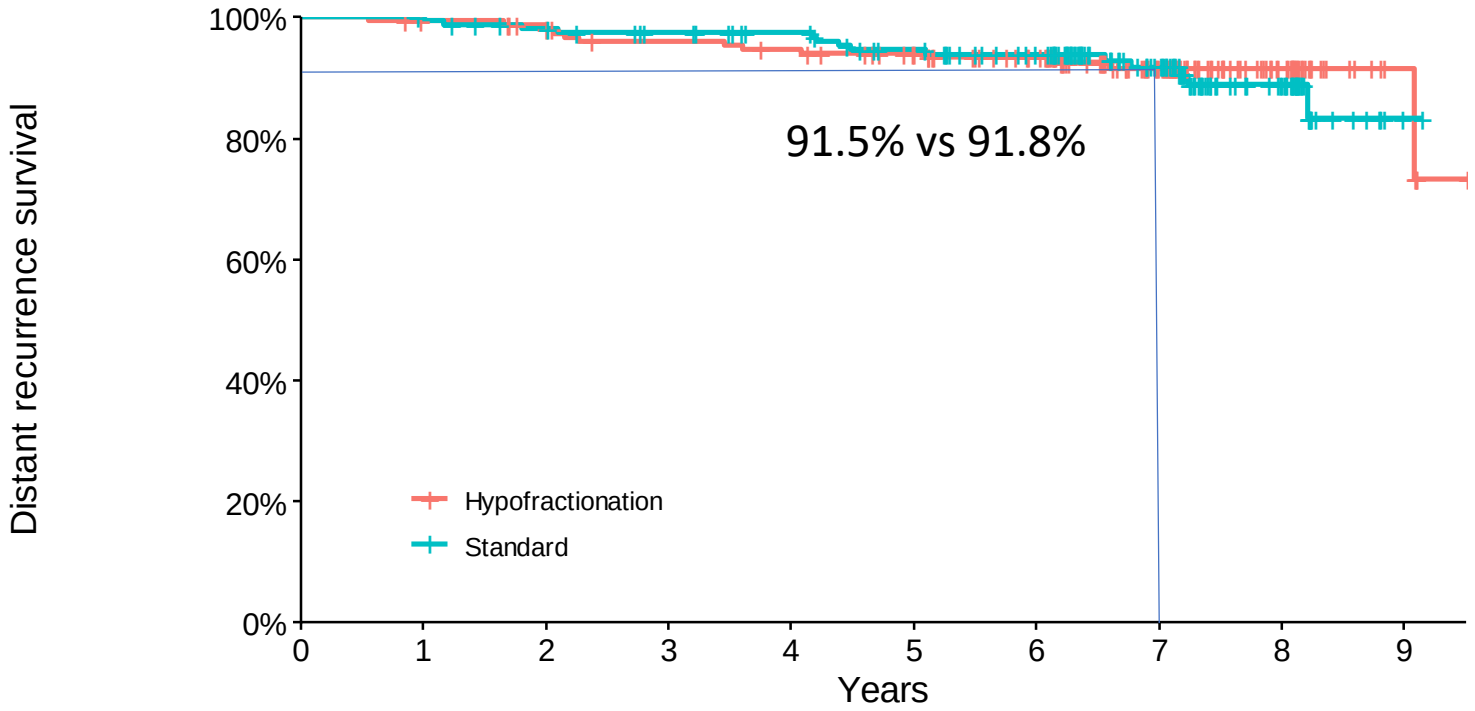
Biochemical failure-free survival



Number at risk

Hypofractionation	158	155	149	145	139	130	115	78	30	4
Standard	160	158	153	146	139	128	111	72	34	1

Distant metastasis-free survival

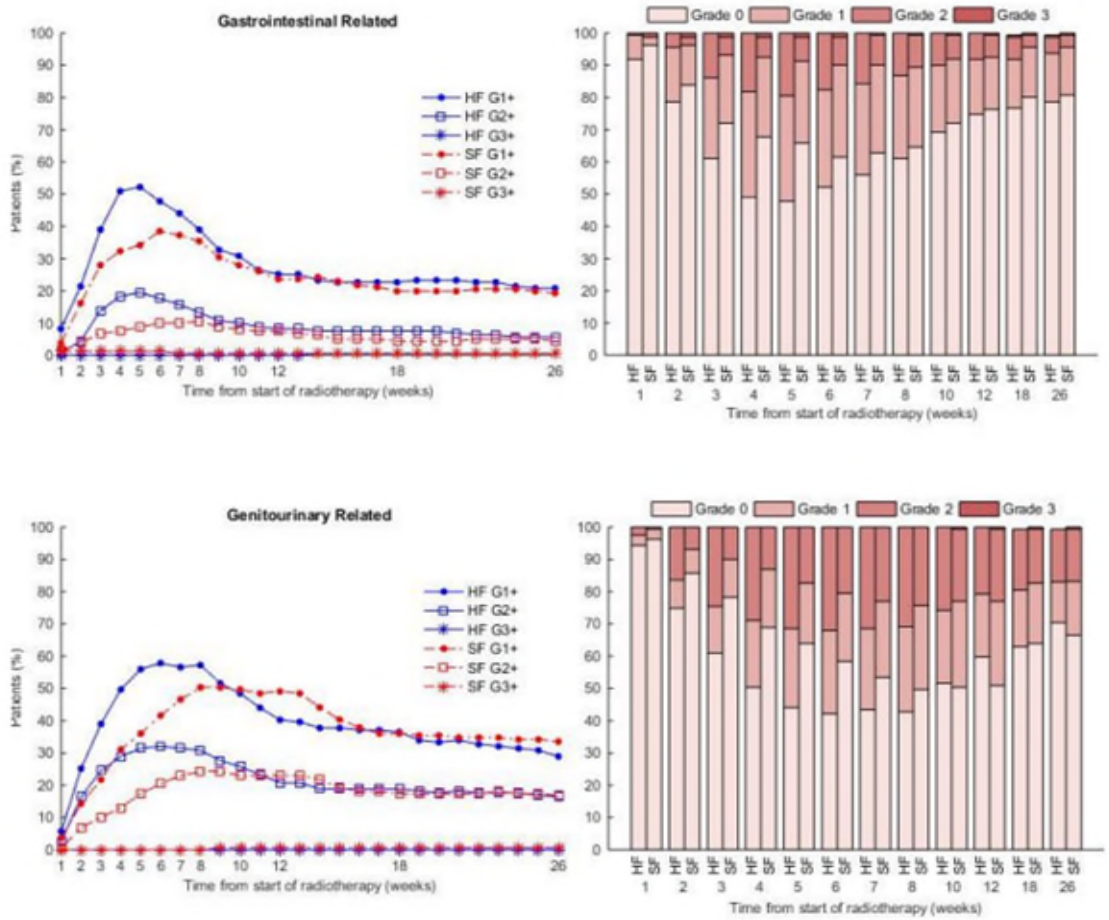


Number at risk

Hypofractionation	158	155	150	144	141	133	119	81	33	5
Standard	160	159	153	147	141	131	118	79	35	1

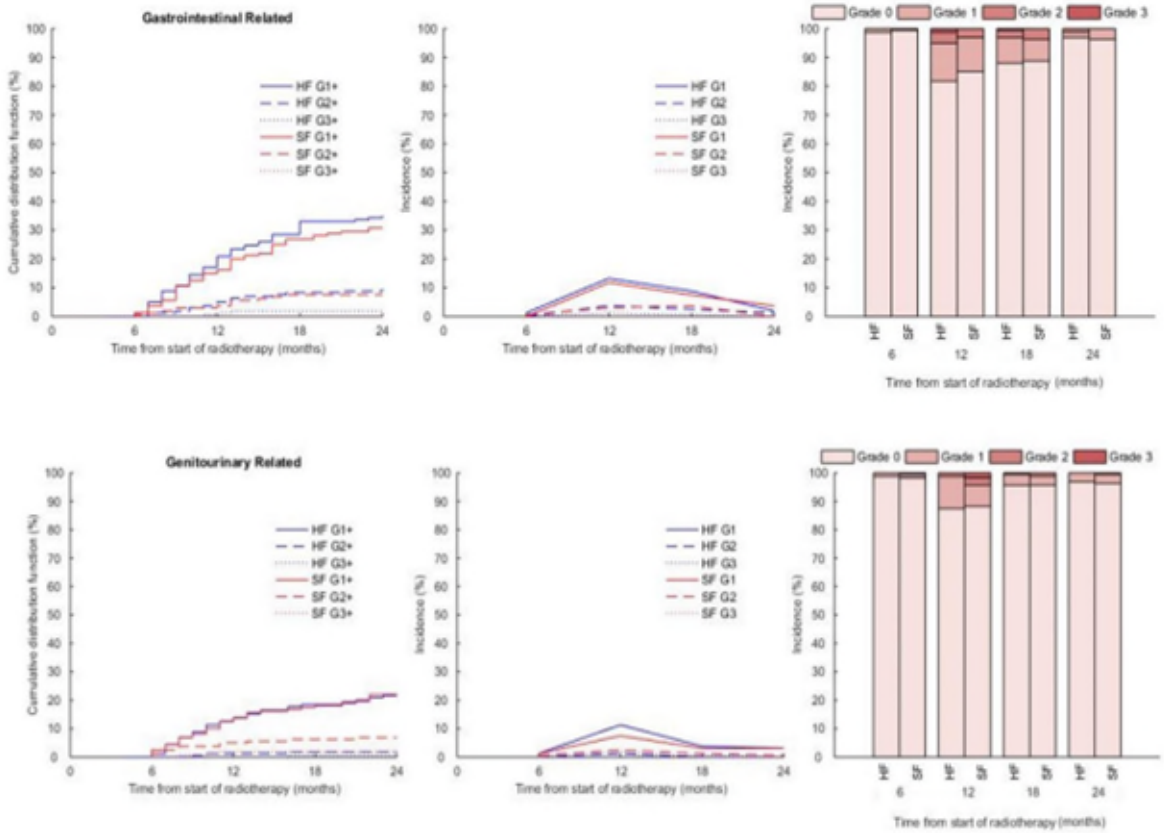
Adverse Events: Acute

Acute Toxicity	Total events	HF	SF	HF vs SF OR	(95% Wald CI)	p value
Gastrointestinal Related						
Grade 1 or worse	185	102	83	1.76	(1.11-2.78)	0.016
Grade 2 or worse	59	37	22	1.92	(1.06-3.47)	0.031
Grade 3 or worse	3	1	2			
Grade 4 or worse	0	0	0			
Genitourinary Related						
Grade 1 or worse	204	105	99	1.28	(0.80-2.04)	0.298
Grade 2 or worse	102	55	47	1.35	(0.84-2.17)	0.222
Grade 3 or worse	1	0	1			
Grade 4 or worse	0	0	0			



Adverse Events: Late

Late Toxicity	Total events	HF	SF	HF vs SF HR	(95% Wald CI)	p value
Gastrointestinal Related						
Grade 1 or worse	104	55	49	1.22	(0.83-1.80)	0.322
Grade 2 or worse	27	15	12	1.32	(0.61-2.83)	0.482
Grade 3 or worse	3	3	0			
Grade 4 or worse	0					
Genitourinary Related						
Grade 1 or worse	69	34	35	1.04	(0.64-1.68)	0.882
Grade 2 or worse	14	3	11	0.25	(0.06-0.81)	0.035
Grade 3 or worse	4	1	3			
Grade 4 or worse	0					



Conclusions

- First moderately hypofractionated RT study in high-risk prostate cancer patients treated with contemporary radiation and LT-ADT.
- Sample size was based on co-primary endpoint. Acute and delayed toxicity, and survival outcomes were analyzed as secondary endpoints
- Survival outcome curves were nearly identical.

Conclusions

- Hypofractionated RT using 68 Gy in 25 fractions is as effective as conventional fractionation using 76 Gy in 38 fractions with similar and acceptable toxicity.

- Moderately hypofractionated RT (68/25) should be considered as a new standard of care for high-risk PCa patients considered for primary EBRT and LT-ADT.

AI & EI: CARING FOR THE PATIENT IN A WIRELESS WORLD

ASTRO ANNUAL 2022 MEETING

Association of prostate-specific antigen screening rates and subsequent metastatic prostate cancer incidence in a national healthcare system

Abstract 298

Presented by:

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Disclosure & Study Team

- Disclosure: I have no conflicts of interest to disclose.

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Background

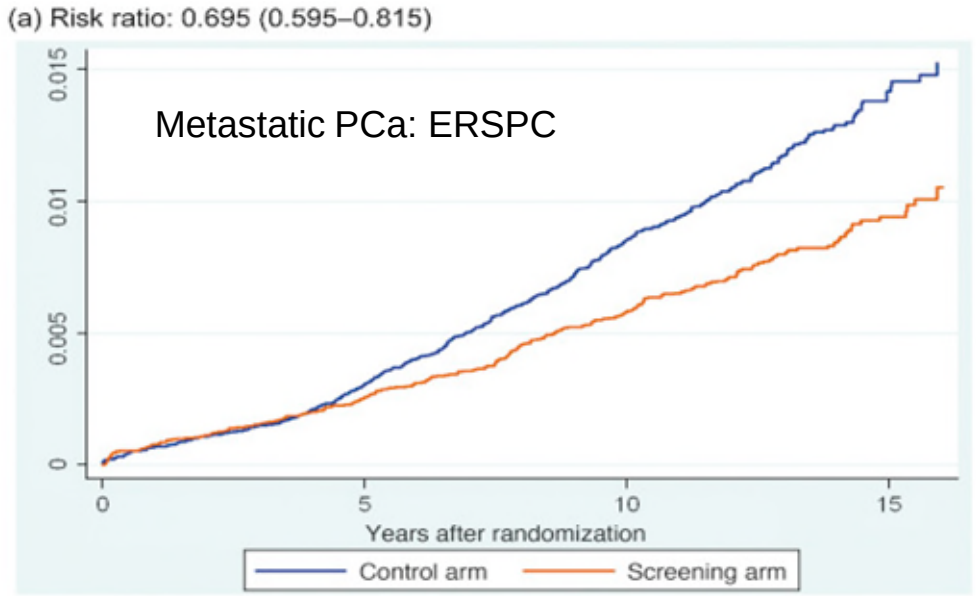
PSA screening is **controversial**.

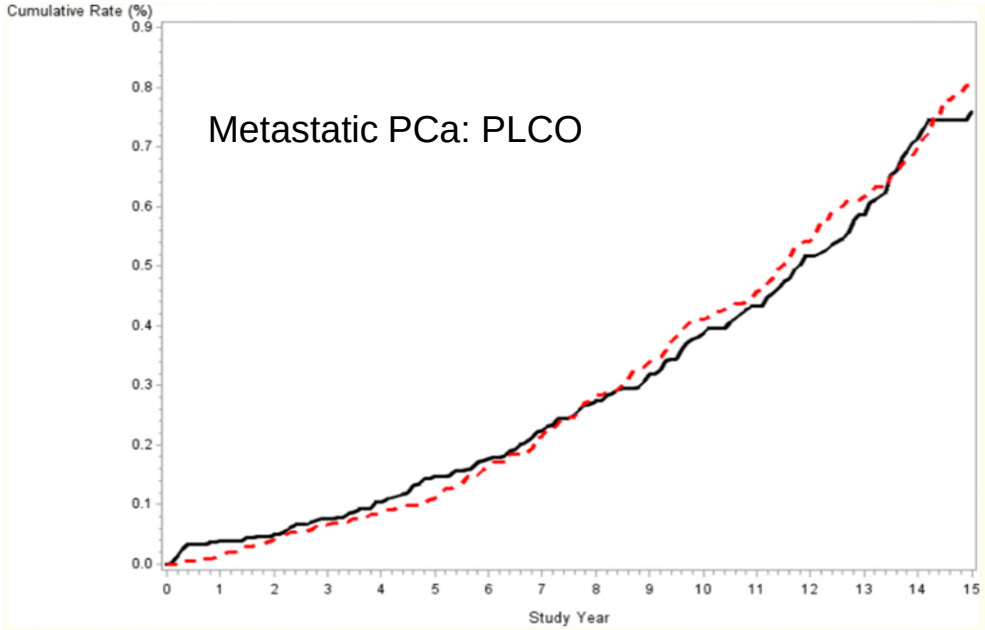
Screening guidelines have changed dramatically.

This has produced **natural variation** in screening.

Metastatic PCa incidence is increasing.

Does natural variation in PSA screening predict metastatic PCa incidence?





Method

128 VA facilities

5M Veterans per year

Exposure 1: yearly facility-level **PSA screening rate** (2005-2014)

Exposure 2: yearly facility-level **long-term non-screening rate** (2005-2014)

Outcome: facility-level, 5-year **lagged metastatic PCa** case count (2010-2019)

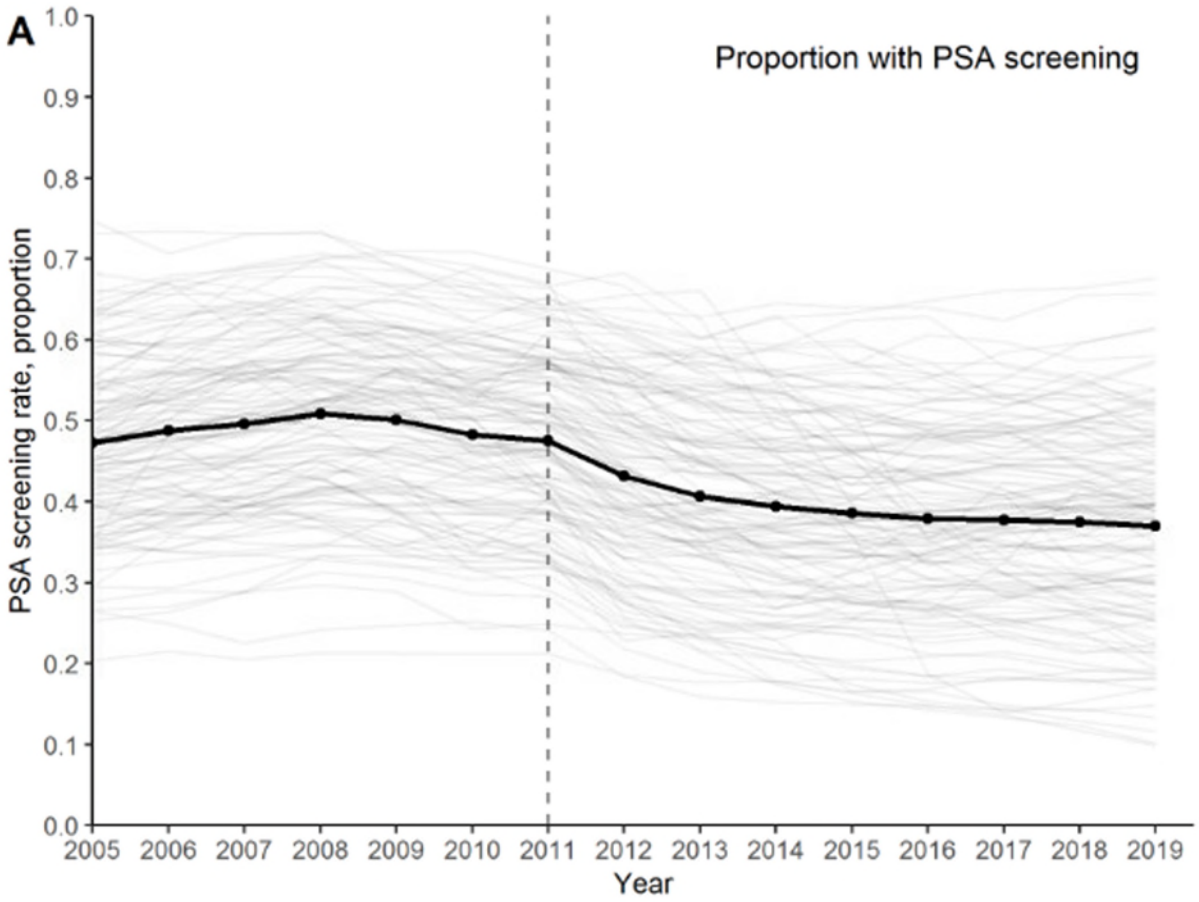
Via natural language processing[1]

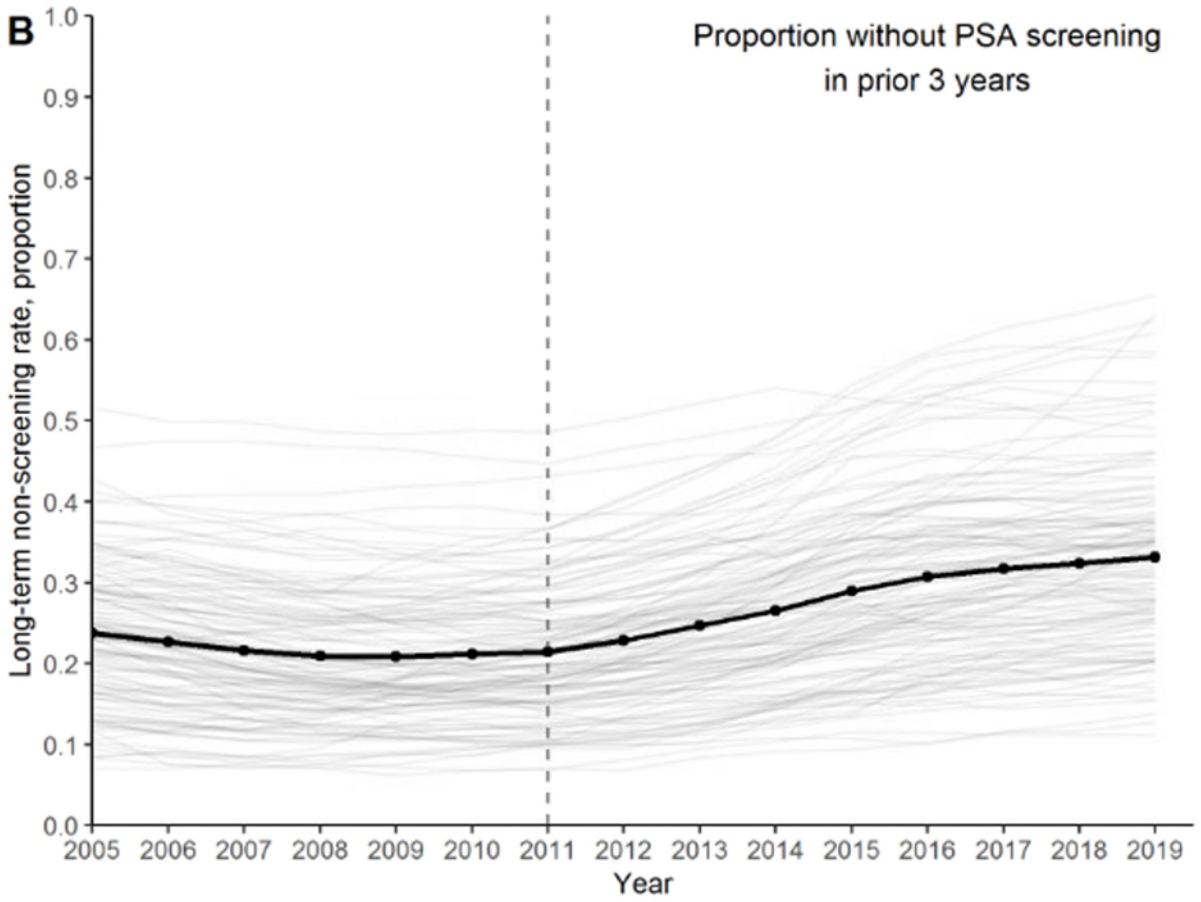
1. Alba PR, Gao A, Lee KM, et al. JCO Clin Cancer Inform 2021;5:1005–14.

Results

PSA screening rates have decreased over time

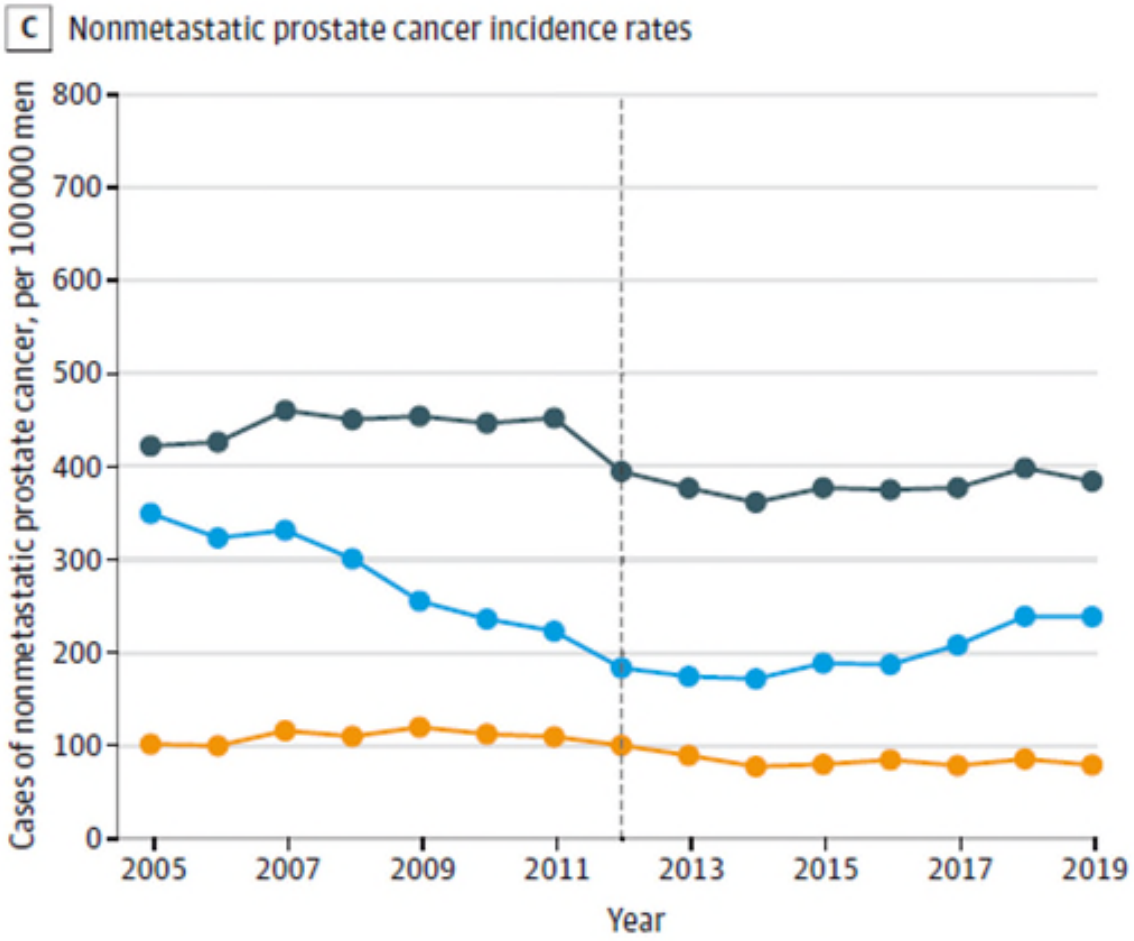
USPSTF draft guidelines recommending against screening for all men

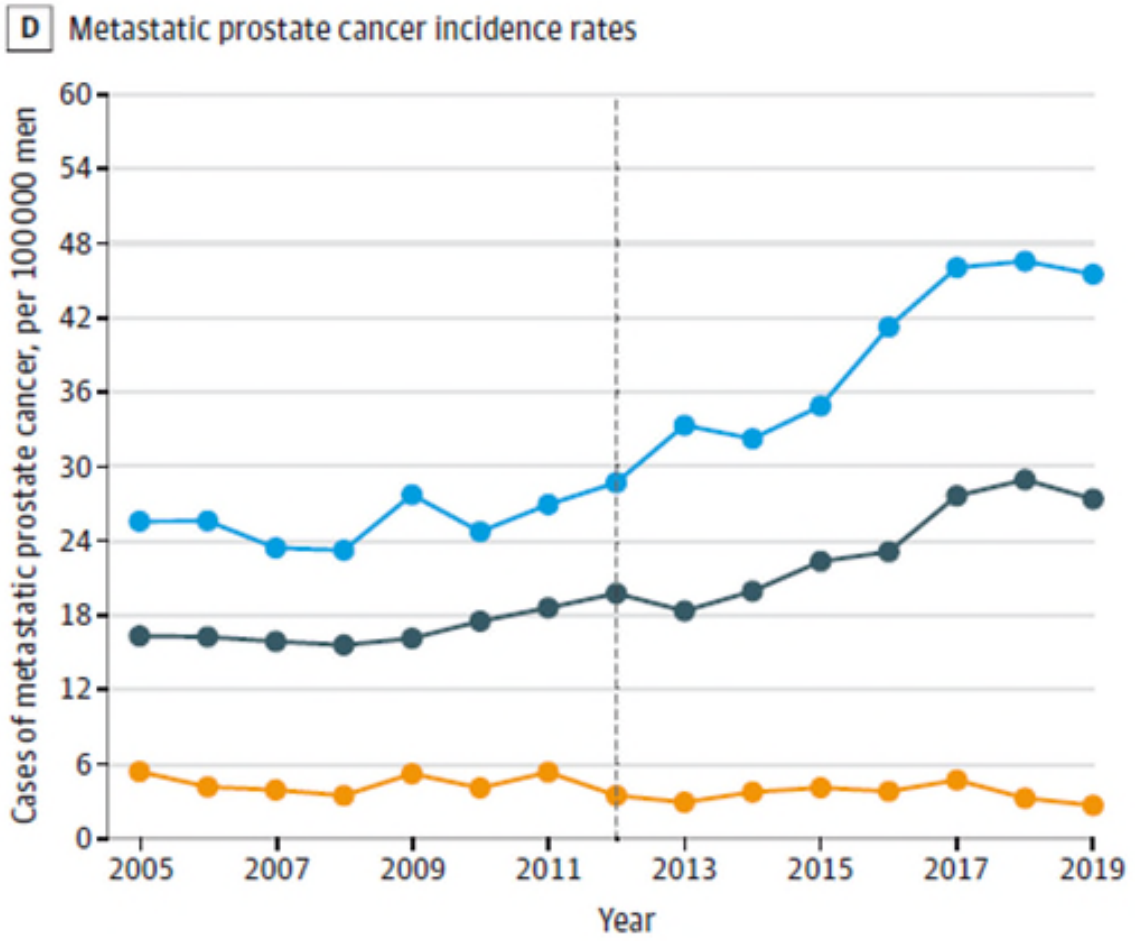




Results

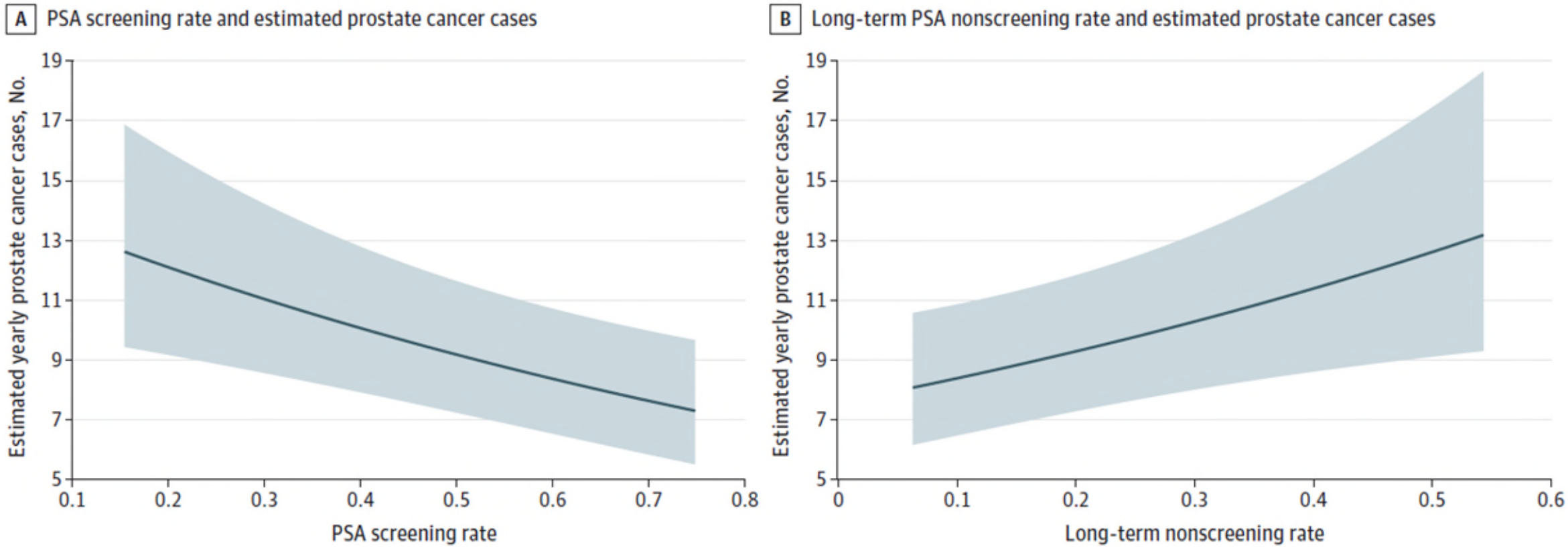
Nonmetastatic PCa has decreased, while metastatic PCa has increased





Results

Facilities with lower PSA screening rates have higher mPCa incidence



Predicted case count estimates were generated from multivariable mixed-effects negative binomial models using a random effect of 0, continuous covariates at their mean values, Pacific region, and facility size of 40 889 men. Shaded areas indicate 95% CIs.

Results

Multivariable model

Table 2. Results of Mixed-Effects Negative Binomial Regressions for Metastatic Prostate Cancer Rates

Variable	Model for PSA screening rate		Model for long-term nonscreening rate	
	IRR (95% CI)[a]	*P* value	IRR (95% CI)[a]	*P* value
PSA screening rate or long-term nonscreening rate[b]	0.91 (0.87-0.96)	<.001	1.11 (1.03-1.19)	.01
Percentage of Black patients, per 10% increase	1.19 (1.09-1.29)	<.001	1.20 (1.11-1.30)	<.001
Calendar year (spline)[c]	NA	<.001	NA	<.001
Percentage of patients aged ≥70 y, per 10% increase	1.12 (0.99-1.27)	.08	1.11 (0.98-1.26)	.10
Availability of novel PET tracers	1.03 (0.95-1.11)	.50	1.02 (0.95-1.11)	.6
Use of MRI of the pelvis for prostate cancer workup, per 10% increase[d]	1.01 (0.97-1.04)	.80	1.00 (0.97-1.04)	.8
Region				
Pacific	1.00 [Reference]	NA	1.00 [Reference]	NA
Continental	0.73 (0.53-0.99)	.04	0.71 (0.52-0.98)	.04
Midwest	0.91 (0.68-1.23)	.60	0.89 (0.66-1.20)	.40
North Atlantic	0.73 (0.54-0.98)	.04	0.71 (0.53-0.96)	.03
Southeast	0.73 (0.52-1.03)	.07	0.70 (0.50-0.99)	.046

Conclusions

PSA screening rates have declined.

Metastatic PCa incidence rates have increased, particularly among 70+ y/o.

VA facilities with lower PSA screening rates had higher subsequent mPCa incidence rates.

Epidemiological evidence supporting **efficacy** of PSA screening in reducing mPCa

Expert Perspective

Jeff M. Michalski,
MD, MBA, FASTRO

Washington University School of Medicine in St. Louis

ASTRO President-elect

AI & EI: CARING FOR THE PATIENT IN A WIRELESS WORLD

ASTRO ANNUAL 2022 MEETING

NRG/RTOG 1112:

Randomized phase III study of sorafenib vs. stereotactic body radiation therapy (SBRT) followed by sorafenib in hepatocellular carcinoma (HCC)

Abstract LBA 01

Presented by:

Laura A. Dawson, MD, FASTRO
Princess Margaret Cancer Centre
University of Toronto

Disclosure & Study Team

NRG ONCOLOGY
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- Disclosure: Bayer, Merck research grants
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Background

- Hepatocellular carcinoma (HCC) is a leading cause of global cancer death
- Standard of care for HCC, unsuitable for surgery, ablation and/or TACE was sorafenib at the time of study inception
  - Sorafenib improves med. survival from 7.9 to 10.7 months.*
  - Less benefit if macrovascular invasion (MVI): med. survival 6.7 to 8.9 months.*
- Integrating radiation strategies in HCC management has been a key question over the past decade, including HCC with MVI.^ +
  - RCT of TARE have not shown a survival benefit, to date (SARAH, SIRvsNIB).^^
- NRG/RTOG1112 was designed to evaluate the role of SBRT plus systemic therapy for HCC in a phase III RCT.

*Llovet et al, SHARP study, NEJM. 2008; ^ Bujold et al. *JCO* 31.13 (2013): 1631-1639; Munoz et al. *Radiot and Oncol* 156 (2021): 120-126; +Yoon SM, et al. *JAMA Oncol.* 2018;4(5):661–669. ^^Vilgrain et al. SARAH. Lancet Oncol 18 (2017); Chow et al. SIRveNIB. J Clin Oncol, 36 (2018)

Hypothesis and Endpoints

Hypothesis: Stereotactic body radiation therapy (SBRT) followed by sorafenib will improve overall survival, compared to sorafenib alone in patients with advanced HCC

Primary endpoint: Overall survival (OS)

Secondary endpoints:

- Progression free survival (PFS)
- Time to progression (TTP) (RECIST)
- Toxicity (CTCAEv4.0)

NRG/RTOG 1112 Schema

Eligibility

- Locally advanced HCC
- Unsuitable for, refractory to or recurrent post resection, RFA or TACE
- Child Pugh A
- Platelets > 60 bil/L
- BCLC stage B or C
- ≤ 20 cm sum of HCC
- ≤ 5 HCC foci
- ≤ 3 cm extrahepatic HCC
- Any degree of vascular invasion

Stratification

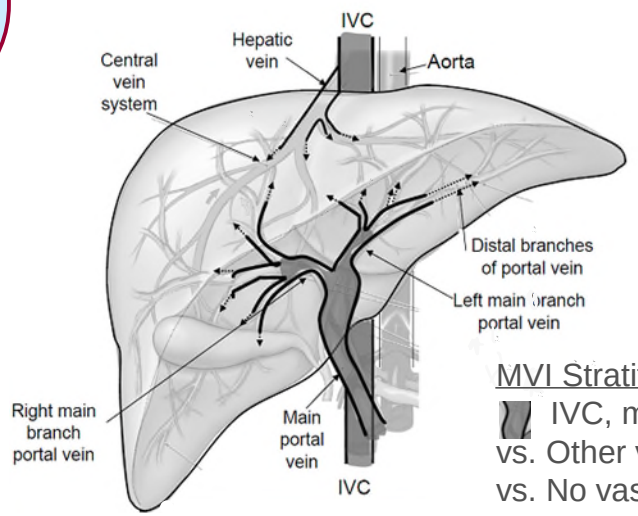
- Macrovascular involvement (MVI) (IVC/main PV R/L PV; other; none)
- Hepatitis B vs. C vs. other
- North American vs. non-North American site
- HCC volume / liver volume (<10%, 10-40%, > 40%)

Randomization

Sorafenib
400 mg po bid

SBRT
27.5 - 50 Gy in 5 fractions

Sorafenib
200 mg po bid x 4 wks, then 400 mg po bid



MVI Stratification

IVC, main portal vein (PV), main R/L PV vascular invasion
vs. Other vascular invasion
vs. No vascular invasion

Statistical Considerations

- Due to changes in HCC SOC systemic therapy, trial closed to accrual with fewer patients than required overall survival (OS) events

Parameters	Prior to Early Accrual Closure	Amendment Post-Early Accrual Closure
Median OS control and experimental arms	10.5 and 14.5 months	10.5 and 14.5 months
Effect size	HR=0.72	HR=0.72
Design	Event driven	Time driven (July 1, 2022 data)
OS events	238	155
Statistical power and α	80% and 1-sided 0.05	65% and 1-sided 0.05
Sample size	292	193

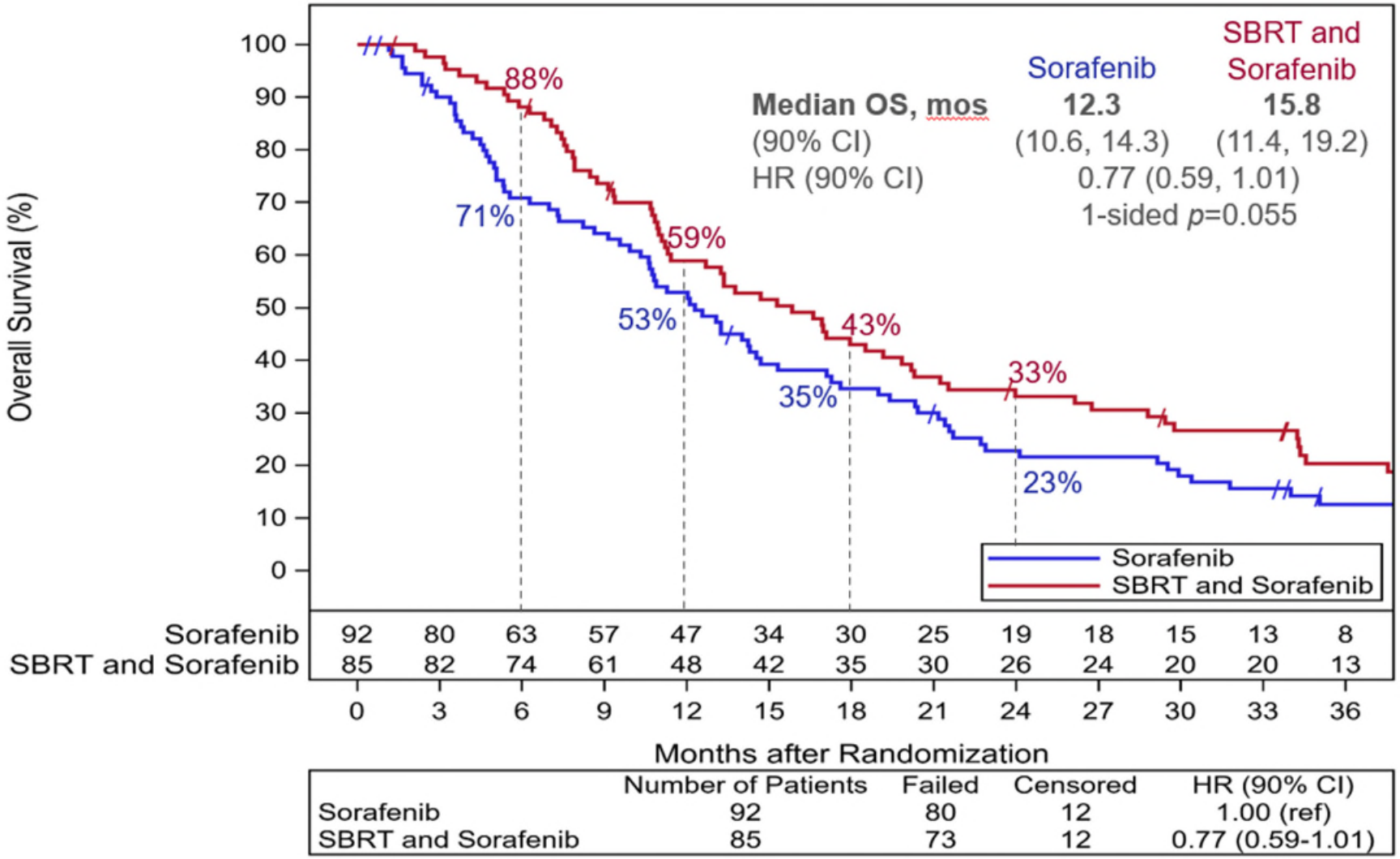
OS estimated by Kaplan-Meier and arms compared using log-rank test. Hazard ratios estimated with Cox models.

Patient and Tumor Characteristics

	Sorafenib (n=92)	SBRT and Sorafenib (n=85)	Total (n=177)
Median Age yrs. (min-max)	67 (27-84)	66 (49-83)	66 (27-84)
Male sex	82 (89%)	68 (80%)	150 (85%)
Zubrod PS^ 1 or 2	51 (55%)	38 (45%)	89 (50%)
Hepatitis C	38 (41%)	35 (41%)	73 (41%)
BCLC Stage C	77 (84%)	68 (80%)	145 (82%)
MVI*	67 (73%)	64 (75%)	131 (74%)
Main, R or L PV	59 (64%)	53 (62%)	112 (63%)
M1	4 (4%)	3 (4%)	7 (4%)

** MVI - macrovascular invasion, R or L PV- right or left main portal vein; ^PS - performance status*

Overall Survival



	Number of Patients	Failed	Censored	HR (90% CI)
Sorafenib	92	80	12	1.00 (ref)
SBRT and Sorafenib	85	73	12	0.77 (0.59-1.01)

Median follow: all patients – 13.2 months; alive patients – 33.7 months

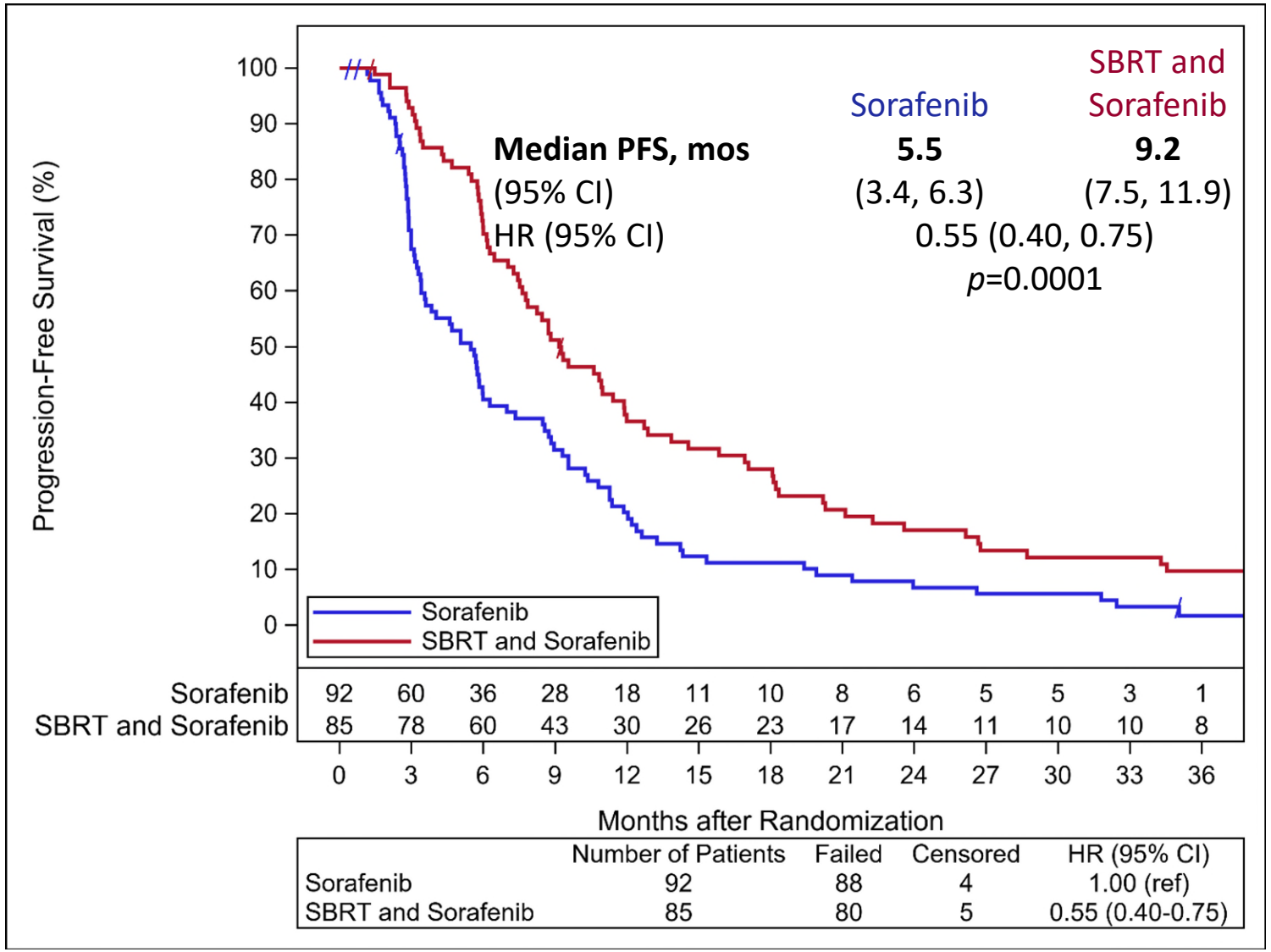
Overall Survival: Multivariable Analysis

Variables	Comparison	HR†	95% C.I. LL	95% C.I. UL	p-value
Treatment	**SBRT and Sorafenib vs. Sorafenib**	**0.72**	**0.52**	**0.99**	**0.042**
Zubrod PS	1 or 2 vs. 0	1.44	1.03	2.01	0.033
Clinical M Stage	M1 vs. M0	2.72	1.24	5.98	0.013
Child Pugh Score	A6 vs. A5	1.48	1.02	2.14	0.038
Macrovascular Involvement	IVC/Main, R main or L main PV vs. Other/None	2.34	1.63	3.34	<0.0001

†Hazard Ratio: HR > 1 indicates an increased risk of failure for the first level of the variable.

Progression-Free Survival

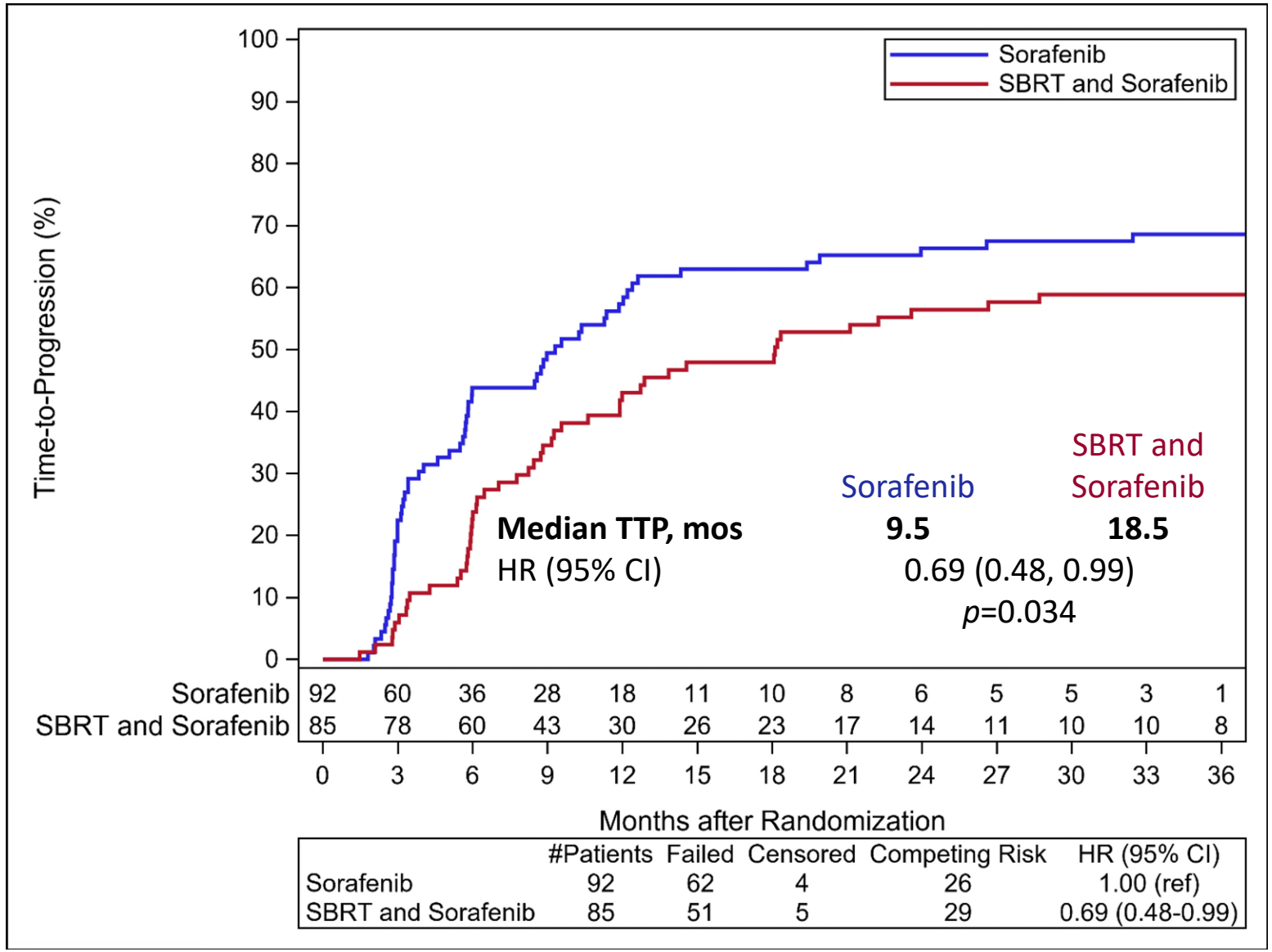
Estimate (95% CI)	Sorafenib (n=92)	SBRT and Sorafenib (n=85)
6-month	41% (30%, 51%)	71% (62%, 81%)
12-month	20% (12%, 29%)	37% (26%, 47%)
18-month	11% (5%, 18%)	28% (18%, 38%)
24-month	7% (2%, 12%)	17% (9%, 25%)



Time to Progression

Estimate (95% CI)	Sorafenib (n=92)	SBRT and Sorafenib (n=85)
6-month	44% (33%, 54%)	23% (14%, 32%)
12-month	57% (46%, 67%)	43% (32%, 53%)
18-month	63% (52%, 72%)	48% (37%, 58%)
24-month	66% (55%, 75%)	56% (45%, 66%)

TTP was estimated with cumulative incidence and arms compared using Gray's test



Adverse Events

	Sorafenib (n=88)	SBRT and Sorafenib (n=83)
	Grades ≥ 3	Grades ≥ 3
Overall Highest AE Grade	**65 (74%)**	**62 (75%)**
GI Bleeds	**5 (6%)**	**3 (4%)**
Esophageal varices hemorrhage	1	0
Gastric/upper gastrointestinal hemorrhage	2	2
Intra-abdominal hemorrhage	1	0
Lower gastrointestinal hemorrhage	0	1
Hepatic hemorrhage	1	0

6 patients excluded: 4 patients did not receive protocol treatment and 2 with no AE data submitted.

Conclusions

- In patients with advanced HCC, compared to sorafenib alone, SBRT prior to sorafenib improved overall survival, progression-free survival, and time to progression.
- SBRT was not associated with an increase in adverse events.
- SBRT is a new standard treatment option for locally advanced HCC, especially with vascular invasion.

Expert Perspective

Karyn A. Goodman,
MD, FASTRO

Icahn School of Medicine at Mount Sinai

AI & EI: CARING FOR THE PATIENT IN A WIRELESS WORLD

ASTRO ANNUAL 2022 MEETING

Examining the Impact of Direct Patient Care for Medical Physicists:

A Randomized Prospective Phase III Trial

Abstract 7

Presented by:

Todd F. Atwood, PhD
University of California, San Diego

Disclosure & Study Team

Disclosure: I have no conflicts of interest to disclose.

Full author list:

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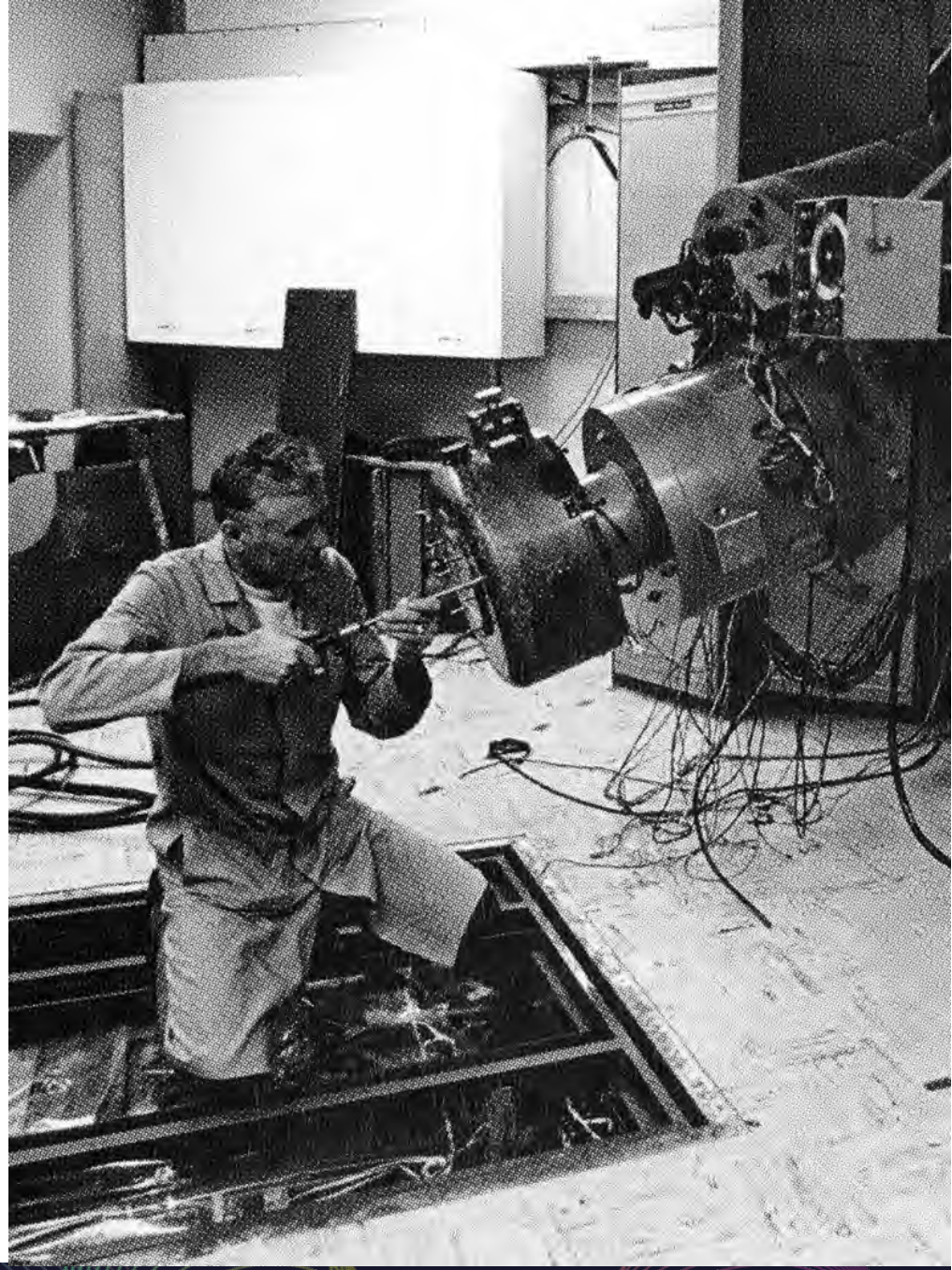
@DrMedPhys

Background

While the primary function of the medical physicist has always centered around the design and delivery of safe and efficacious therapy

The day-to-day responsibilities of medical physicists have consistently evolved to meet the changing needs of patients and the field



Background

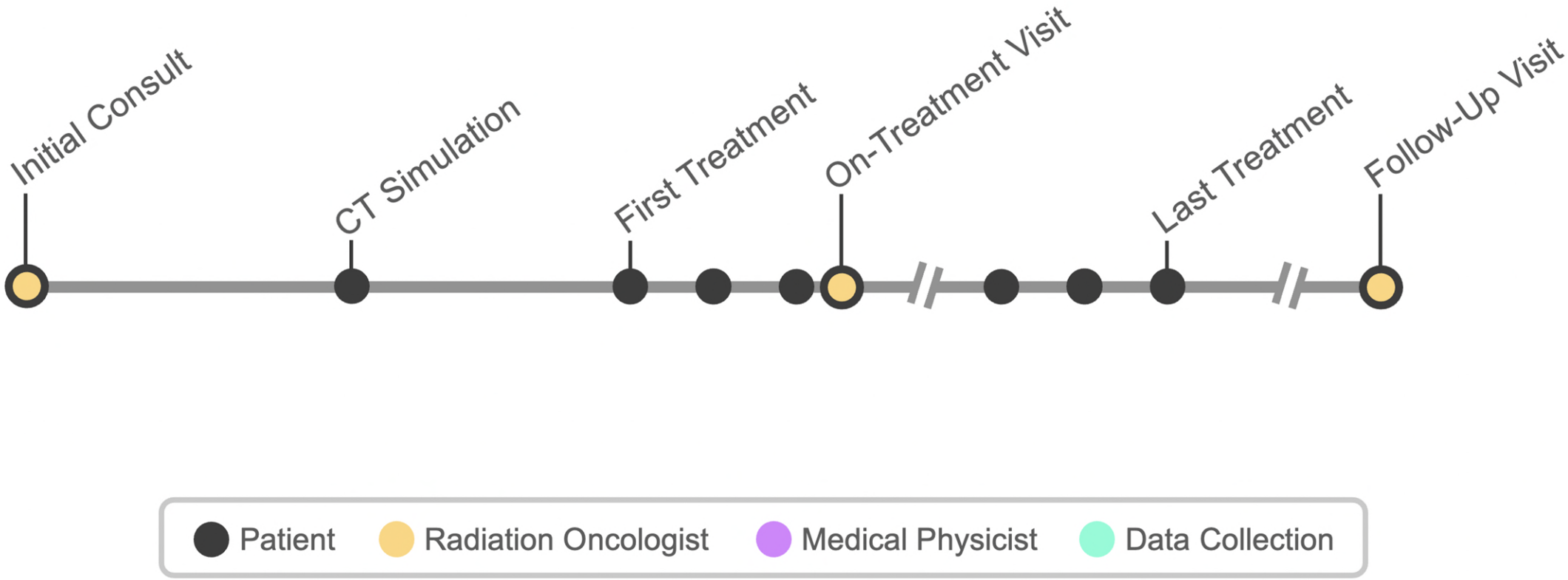
More patients are searching for ways to be involved in their care[1,2]

Available patient information is too complex for the general population[3,4,5]

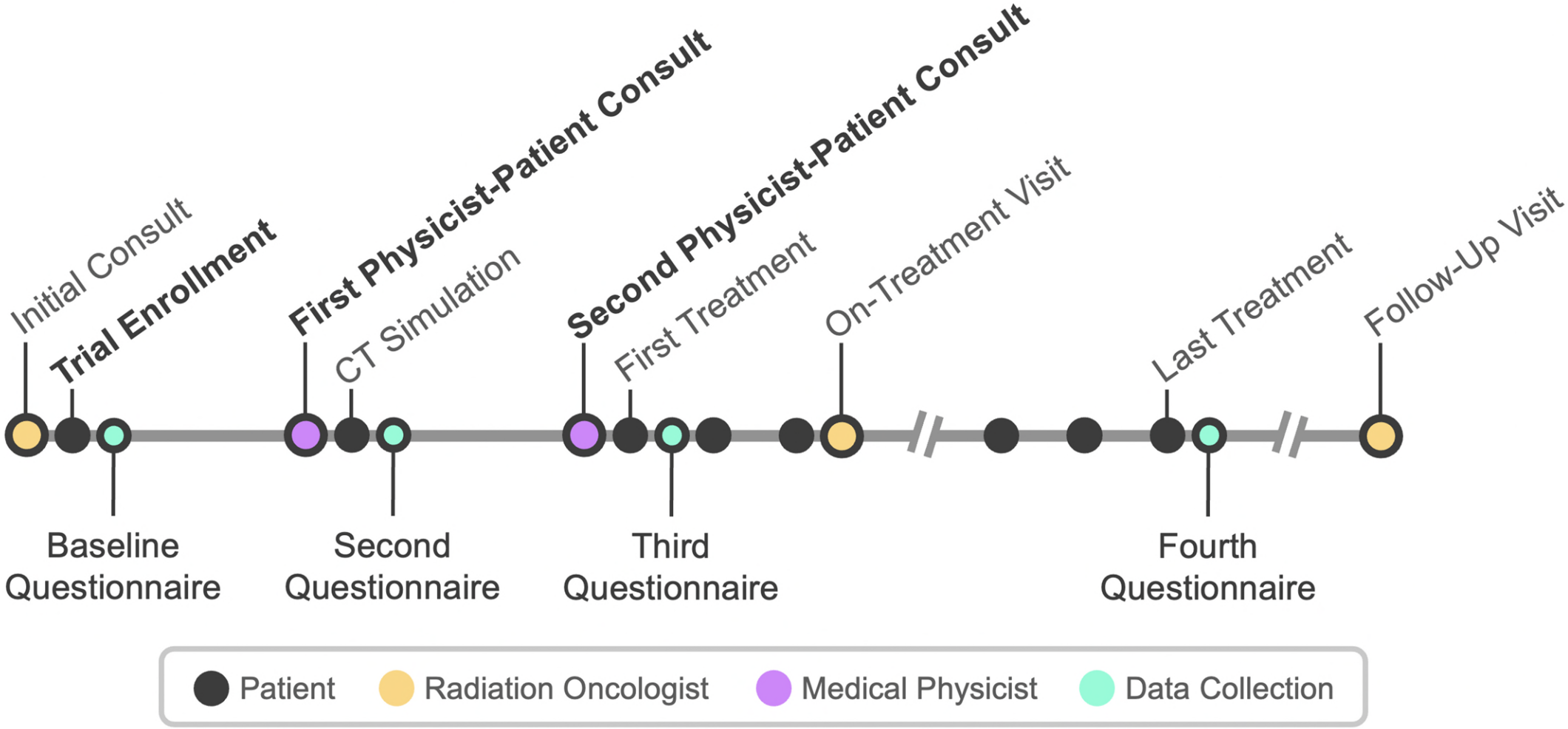
Patient related distress can negatively impact outcomes following radiation therapy[6]

1. Rutten L, et al. *Patient Educ Couns* (2005)
2. Zeguers M, et al. *Int J Radiat Oncol Biol Phys* (2012)
3. Byun J, et al. *Int J Radiat Oncol Biol Phys* (2015)
4. Rosenberg S, et al. *Pract Radiat Oncol* (2017)
5. Rooney MK, et al. *Pract Radiat Oncol* (2019)
6. Habboush Y, et al. *Adv Radiat Oncol* (2017)

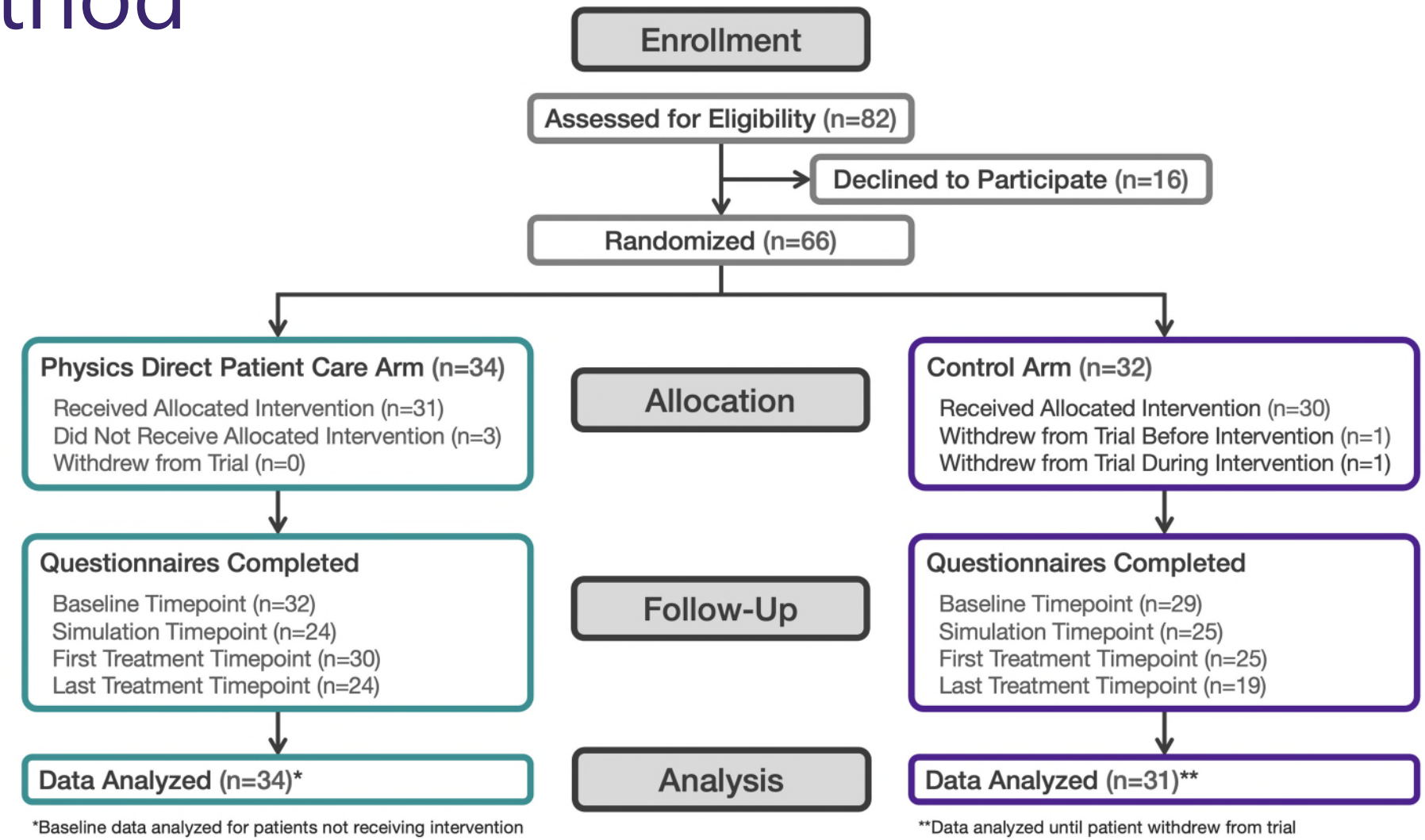
Method


Initial Consult
CT Simulation
First Treatment
On-Treatment Visit
Last Treatment
Follow-Up Visit
Patient
Radiation Oncologist
Medical Physicist
Data Collection

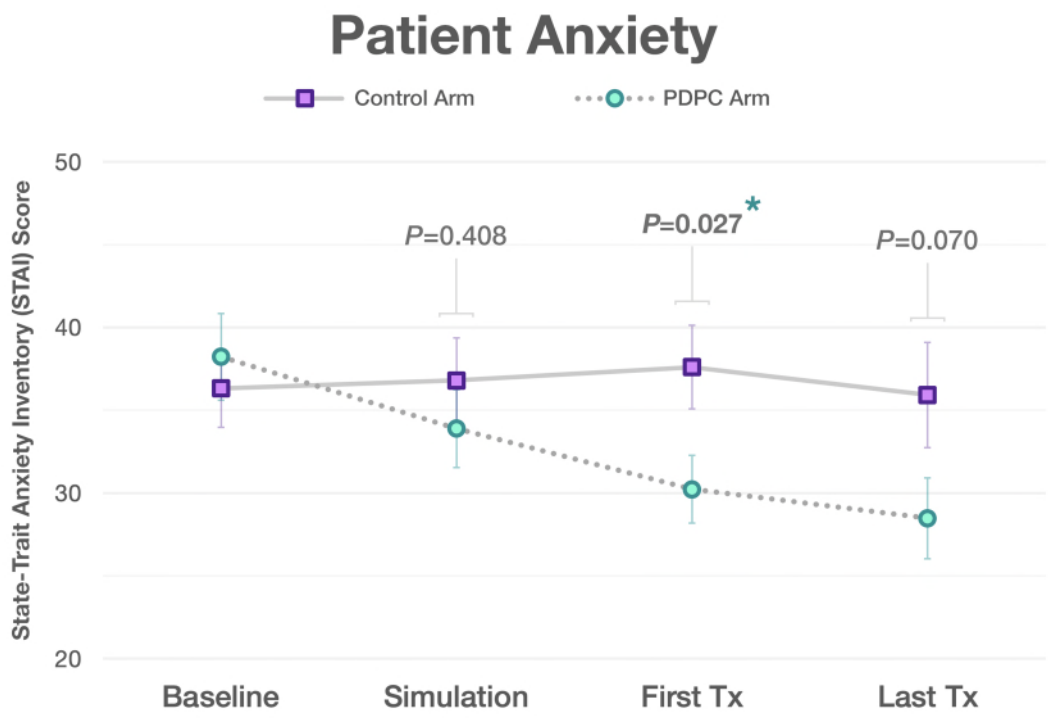
Method

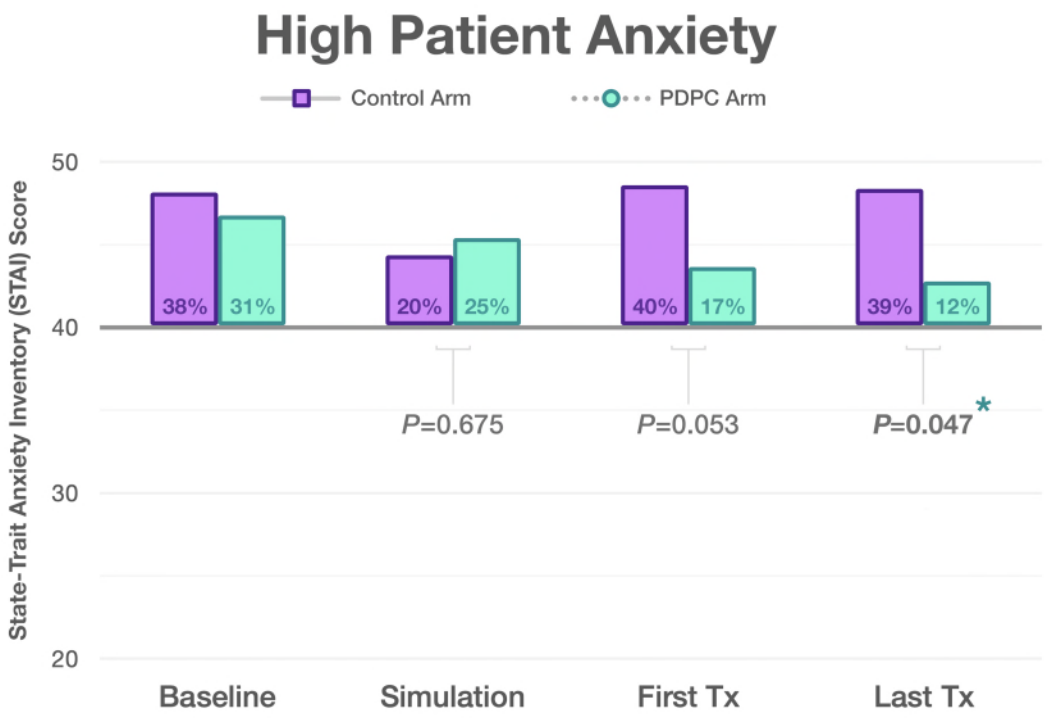

Initial Consult
Trial Enrollment
First Physicist-Patient Consult
CT Simulation
Second Physicist-Patient Consult
First Treatment
On-Treatment Visit
Last Treatment
Follow-Up Visit
Baseline Questionnaire
Second Questionnaire
Third Questionnaire
Fourth Questionnaire
Patient
Radiation Oncologist
Medical Physicist
Data Collection

Method

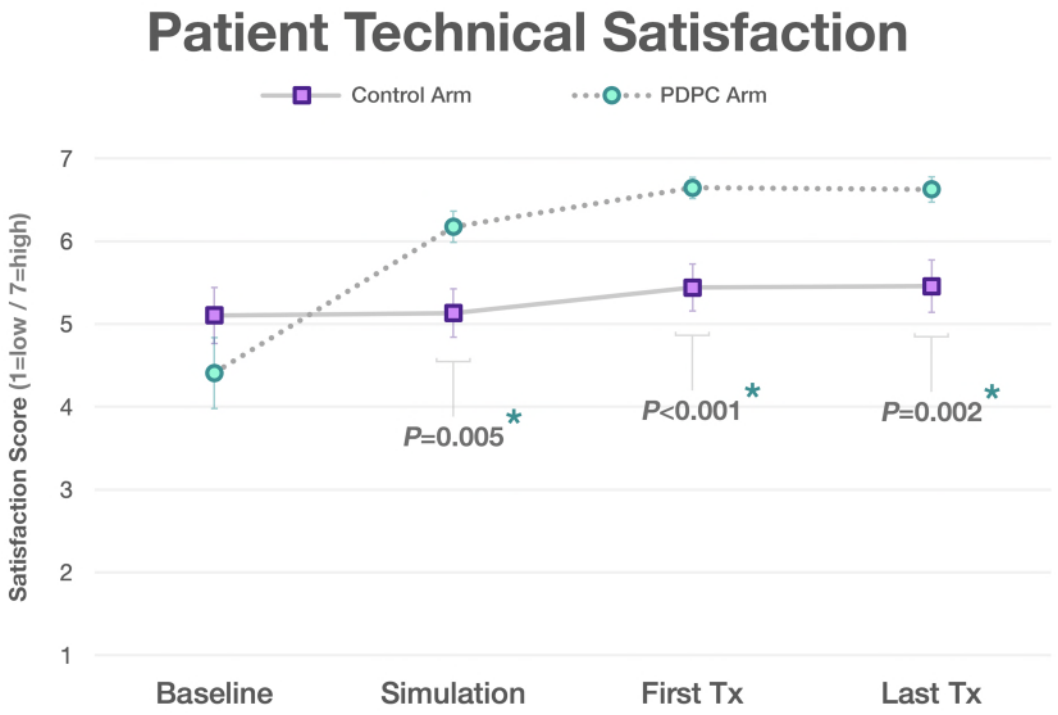

Enrollment
Assessed for Eligibility (n=82)
Declined to Participate (n=16)
Randomized (n=66)
Physics Direct Patient Care Arm (n=34)
Received Allocated Intervention (n=31)
Did Not Receive Allocated Intervention (n=3)
Withdrew from Trial (n=0)
Allocation
Control Arm (n=32)
Received Allocated Intervention (n=30)
Withdrew from Trial Before Intervention (n=1)
Withdrew from Trial During Intervention (n=1)
Questionnaires Completed
Baseline Timepoint (n=32)
Simulation Timepoint (n=24)
First Treatment Timepoint (n=30)
Last Treatment Timepoint (n=24)
Follow-Up
Questionnaires Completed
Baseline Timepoint (n=29)
Simulation Timepoint (n=25)
First Treatment Timepoint (n=25)
Last Treatment Timepoint (n=19)
Data Analyzed (n=34)*
Analysis
Data Analyzed (n=31)**
*Baseline data analyzed for patients not receiving intervention
**Data analyzed until patient withdrew from trial

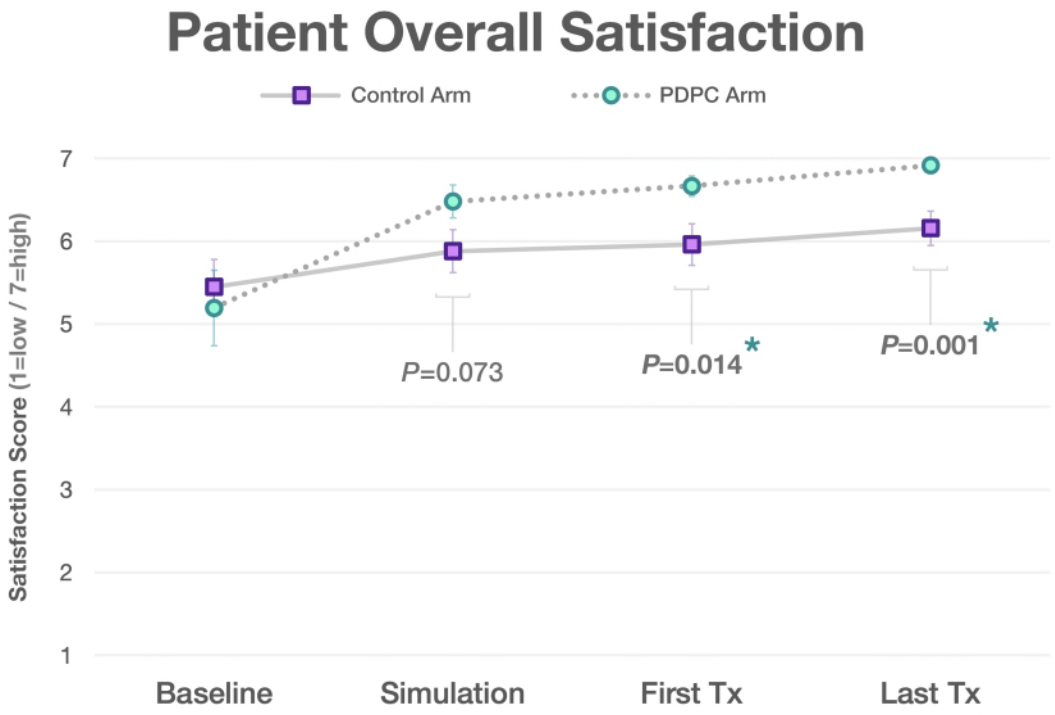
Results: Patient Anxiety





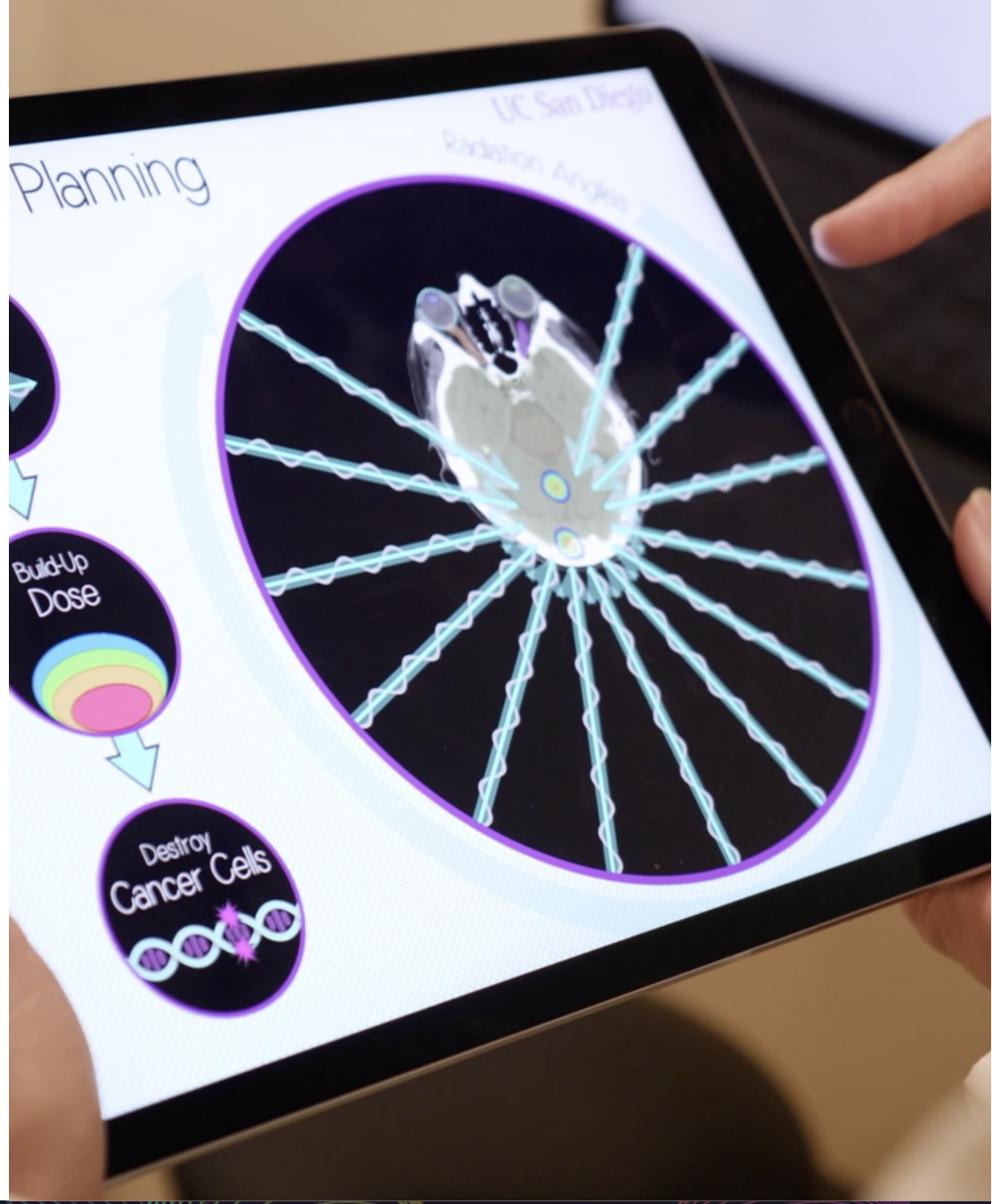
Results: Patient Satisfaction





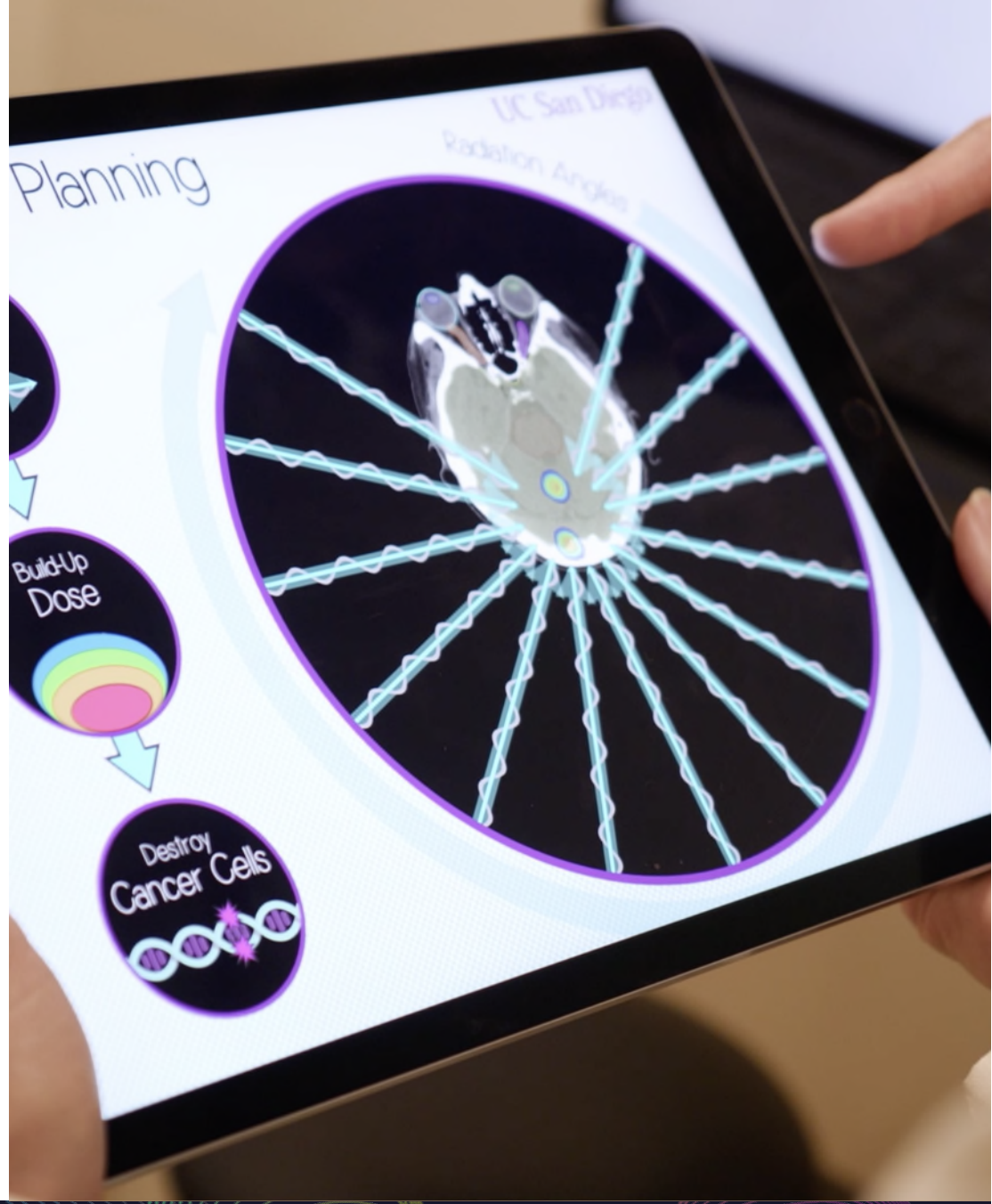
Conclusions

Significant improvements in anxiety, technical satisfaction, and overall satisfaction for patients receiving physicist-patient consults compared to patients receiving the standard of care



Conclusions

Expanding the scope of the medical physics profession to include new patient-facing responsibilities allows us to add more value to the field and provide better care for our patients



AI & EI: CARING FOR THE PATIENT IN A WIRELESS WORLD

ASTRO ANNUAL 2022 MEETING

FAST-01:

Results of the first-in-human study of proton FLASH radiotherapy

Abstract 6

Presented by:

Emily C. Daugherty, MD

University of Cincinnati Cancer Center & Cincinnati Children's Hospital Medical Center

Disclosure & Study Team

- Employer: University of Cincinnati/UC Health
- Disclosure: I have received honoraria from Varian Speakers Bureau
- This study was supported by funding from Varian, a Siemens Healthineers Company

Full author list:
E. C. Daugherty[1], A. E. Mascia[1,2], M. G. B. Sertorio[1], Y. Zhang[1,2], E. Lee[1,2], Z. Xiao[1,2], J. Speth[1,2] J. Woo[3], C. McCann[3], K. Russell[3], L. Levine[3], R. Sharma[3,5], D. Khuntia[3], J. D. Bradley[4], C. B. Simone II[5], J. P. Perentesis[1,2], and J. C. Breneman[1,2];
[1]University of Cincinnati Medical Center, Cincinnati, OH, [2]Cincinnati Children's Hospital, Cincinnati, OH, [3]Varian Medical Systems, Inc., Palo Alto, CA, [4]University College London Hospital, London, UK, [5]Winship Cancer Institute, Emory University, Atlanta, GA, [6]New York Proton Center, New York, NY,

Background

- Side effects of conventional radiation to surrounding organs at risk limit the amount of dose we can utilize to treat cancer
- FLASH treatment delivers radiation at ultra-high dose rates, approximately 1000 times faster than those used currently in practice
- Preclinical studies show that FLASH-RT (over 40 Gy/second) can reduce injury to normal tissues compared to radiotherapy delivered at standard dose rates (1-2 Gy/minute)
- To date, only one patient worldwide has been treated with electron FLASH
- **Purpose**: assess the workflow feasibility, toxicity, and efficacy of proton FLASH radiotherapy for the treatment of painful bone metastases in the extremities

Method

- **Design**: Prospective feasibility study
- **Study population**: 10 subjects with 1 to 3 painful bone metastases in the extremities treated using FLASH radiotherapy
  - Rx dose and fractionation same as standard of care for palliation of bone metastases: 8 Gy in 1 treatment
- **Primary Objectives**:
  - Workflow Feasibility
  - Toxicity
- **Secondary Objective**: Pain Relief
- **1 investigational site:** Cincinnati Children's/UC Health Proton Therapy Center
- **Study Timeline:** expected to take 12 mo; completed November 2020 – October 2021

Results

- 10 patients
  - 5 male/5 female
- Median age:
  - 63 years
- All white, non-Hispanic
- 12 metastatic sites

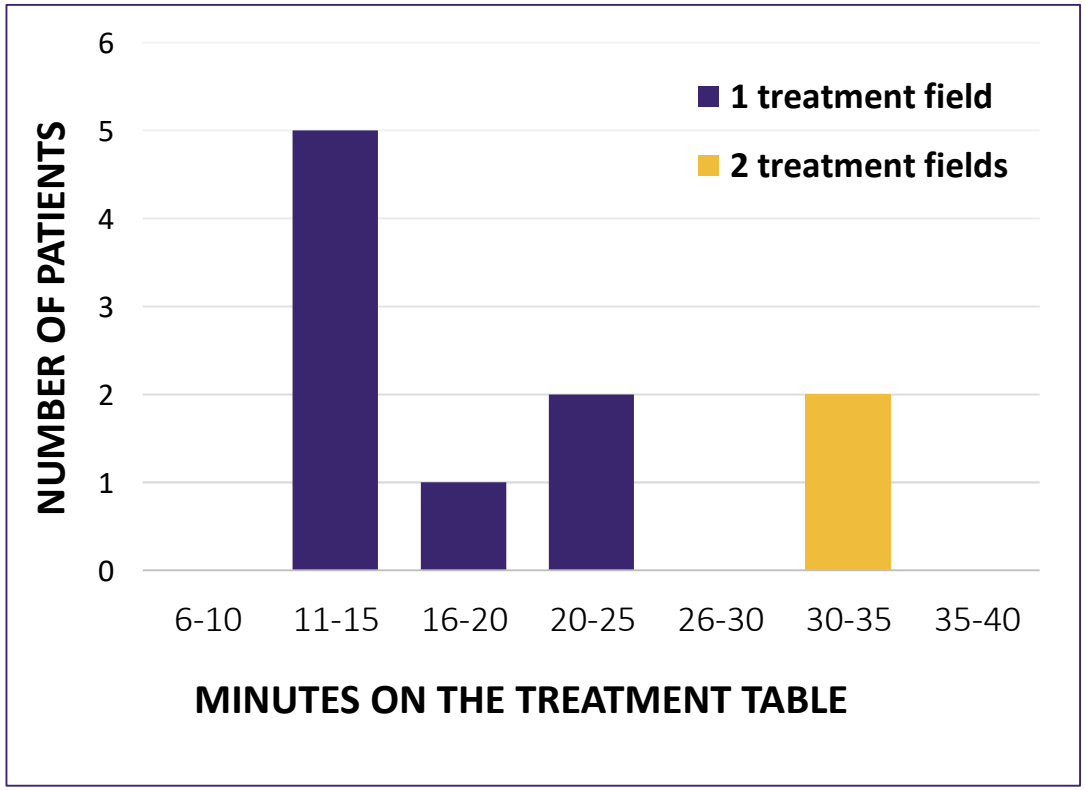
Primary Malignancy	# of Patients
Lung	3
Breast	2
Multiple Myeloma	2
Prostate	1
Thyroid	1
Other	1

FLASH Treatment Sites	# of Treatments
Femur	5
Humerus	5
Tibia	2
TOTAL	12

Results

- No FLASH-related technical issues
- No FLASH-related delays occurred

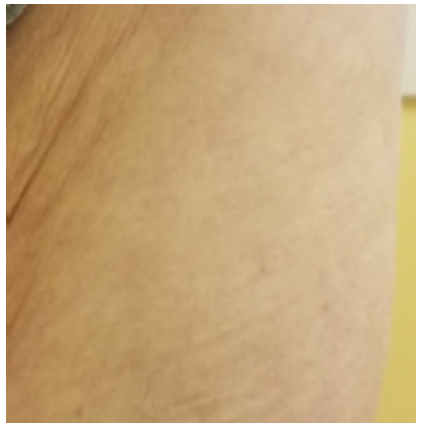
- Median time patient was on treatment table: 13 minutes

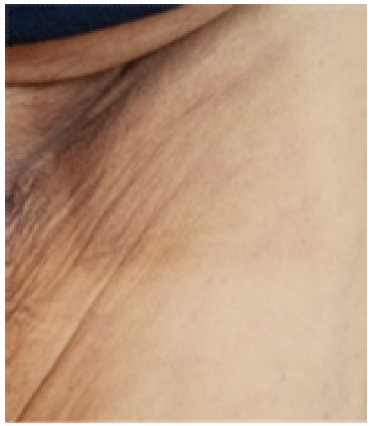


Results

- **There were no serious adverse events related to FLASH**

- Most common side effect was transient, mild hyperpigmentation (n=4)


Before FLASH


2 months post-FLASH


5 months post-FLASH

Adverse Events attributed* to FLASH	n
Acute (<= 3 months post-treatment)	
Edema, limb (G1)	1
Erythema (G1)	1
Extremity pain (G2)	1
Fatigue (G1)	1
Pruritis (G1)	2
Skin hyperpigmentation (G1)	4
Long-term (>3 months post-treatment)	
Skin discoloration (G1)	1

*Possibly, probably, or definitely related, per investigator

Results

- Pain responses, the incidence of pain flare, and re-treatment rates comparable to conventional palliative radiotherapy

Bone Pain Relief Response	# treatment sites	% treatment sites
Complete Response (no pain score at treatment site at 3 months)	**6**	**50%**
Partial Response (reduced pain score at treatment site at 3 months)	**2**	**17%**
Stable Disease	3	25%
Progressive Disease	1	8%
TOTAL	12	100%

Results

Pain Flare

- **4/12 (33%)** of treated sites (or 4/10 = 40% of subjects)
  vs. Chow, et al. **35%** subjects experienced pain flare (non-dexamethasone group)

Re-treatment

- 2/12 sites required re-treatment for rate of **17%** (or 2/10 = 20% of subjects)
  vs. RTOG 9714 with re-treatment rate of **18%** of subjects in 8 Gy arm

- No evidence for decreased durability of response with FLASH

Conclusions

- FLASH is a promising, potentially practice-changing treatment modality
- FAST-01 confirms workflow feasibility of delivering FLASH proton radiotherapy in the clinic
- Treatment efficacy and toxicity of FLASH are both comparable to current conventional palliative RT
- Future trials (FAST-02) are underway to utilize proton FLASH in other areas of the body

	FAST-01 proton FLASH therapy (% subjects)	Conventional dose-rate photon RT (% subjects)
Pain flare	40%	35%[1]
Overall response	70%	65%[2]
Retreatment	20%	18%[2]

[1]Chow et. al., *Lancet Oncol*, Vol. 16 Issue 15 pp 1463-1472, 2015.
[2]Hartsell et al. *J Natl Cancer Inst,* Vol. 97 Issue 11 pp 798-804, 2005.

Expert Perspective

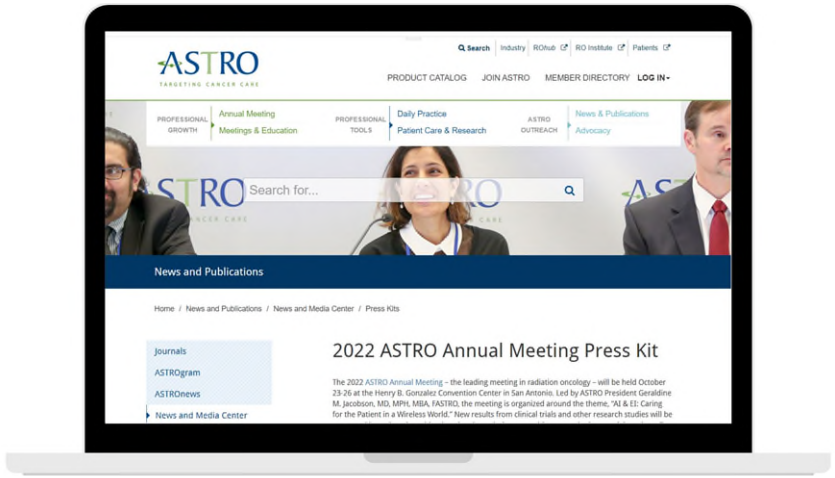
Julianne M. Pollard-Larkin, PhD

The University of Texas
MD Anderson Cancer Center

Q&A Session

Please submit your questions in the chat, including your name/outlet, or raise your hand to ask via audio.

ASTRO ANNUAL 2022 MEETING



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