A decorative graphic on the left side of the slide. It consists of a fan of yellow lines radiating from a central point, with a white crosshair overlaid on it. The crosshair has a vertical line and a horizontal line that intersect at the center of the fan.

Patient Reported Outcomes and Building a Career in Science

Deborah Watkins Bruner, RN, PhD, FAAN
Robert W. Woodruff Professor of Nursing
Director, Faculty Mentorship
Nell Hodgson Woodruff School of Nursing
Professor of Radiation Oncology
Associate Director for Mentorship, Education
and Training
Winship Cancer Institute
Emory University

Patient Reported Outcomes Give Voice to the Patient Experience and Provide:

- △ More comprehensive reporting of prevalence of symptoms
- △ Improved accuracy in reporting of levels of severity
- △ Increased prognostic specificity
- △ Greater understanding of patient adherence
- △ Better information for patient and clinical decision making
- △ Additional targets for labeling claims
- △ Significant information for comparative effectiveness
- △ Information to guide endpoints in Phase I, II and III clinical trials including Precision Medicine

Definitions

PRO

“A Patient Reported Outcome (PRO) is a measurement of any aspect of a patient’s health status that comes directly from the patient (i.e. without interpretation of the patient’s responses by a physician or anyone else).”

U.S. Department of Health and Human Services,
<http://www.fda.gov/cder/guidance/>, 2009

VS

CTC-AE

The NCI Common Terminology Criteria for Adverse Events v4.0 is a descriptive terminology which can be utilized for Adverse Event (AE) reporting. A grading (severity) scale is provided for each AE term.

http://www.acrin.org/Portals/0/Administrati on/Regulatory/CTCAE_4.02_2009-09-15_QuickReference_5x7.pdf

PROs Show Discrepancy Between Clinician-Patient Rated Symptom Severity

RTOG's First QoL Study: RTOG 90-20 Phase II Trial of EBRT + Etanidazole for Locally Advanced Prostate Cancer

- △ Compare patient self-report of the same symptoms used by medical professional ratings
- △ Disagreement between patient and medical professional ratings for symptoms of dysuria, diarrhea and erectile dysfunction. 13% to 45% at 3 months.
- △ RTOG determined this was a significant finding in clinical trials.



Prognostic Value of PROs

- △ Baseline EORTC-QLQ score in **NSCLC** RTOG clinical trial
 - Replaced known prognostic factors (KPS, stage, sex, age, race, marital status, histology, tumor location) as the sole predictor of long-term OS
 - 10-point higher baseline global QOL score corresponded to a decrease in the hazard of death by approximately 10% (p=.004)
(Movsas et al JCO 2009)

- △ Baseline EORTC-QLQ score in **esophageal cancer**
 - At 2 mos after RT, PRO dysphagia scale was most significant survival predictor.
 - 2-yr survival rate was 54.5% for pts without dysphagia 2 mos after RT compared with 14.3% for those with dysphagia (p <0.001)
(Fang et al IJROBP; 58(5): 2004)

- △ Baseline HRQOL prognostic for survival in:
 - **Cervical Cancer** GOG clinical trial (Monk et al JCO;23(21):2005)
 - **Non-Metastatic breast cancer** (Efficace et al Eur J Cancer;40(7):2004)
 - **Advanced bladder cancer** (Roychowdhury et al JCO; 21(4):2003)

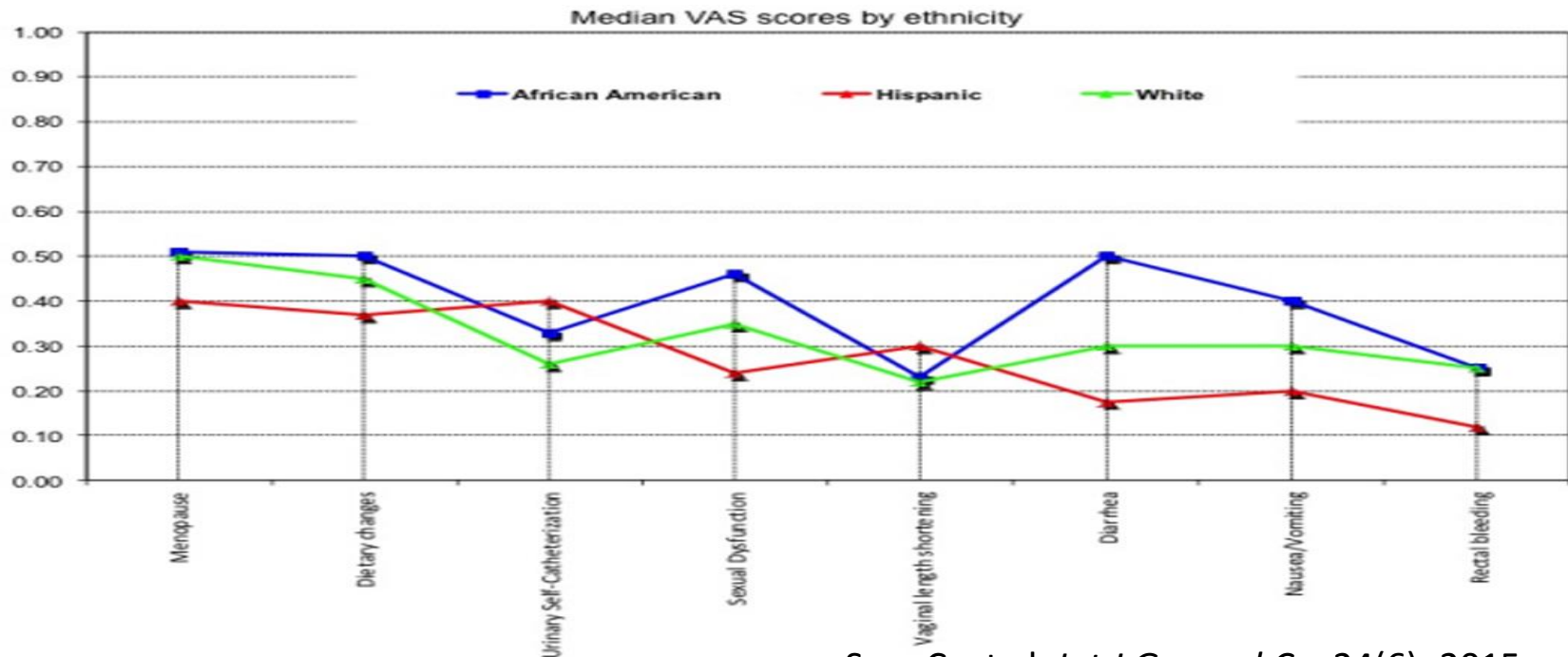
PROs Inform Patient Decision-Making

Study of preferences/utilities of 57 men with Prostate Ca treated with 3DCRT

- Men showed increased preference for health states associated with RT compared with surgery or hormonal therapy.
- Predictors of preference included income, marital status, more aggressive therapy and better prognostic indicators.
- Current quality-of-life scores in terms of global, sexual, or urinary function were poor predictors of preferences.

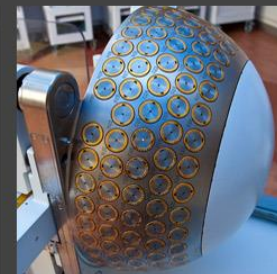
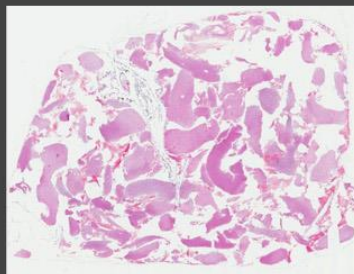
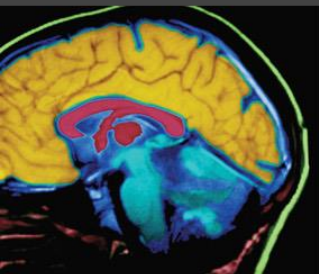
Watkins Bruner, D., et al (2004). *IJROBP*, 58(1):2004

Patient preferences for side effects associated with cervical ca treatment



Sun, C, et al, *Int J Gynecol Ca.* 24(6): 2015

PROs May Inform Comparative-Effectiveness



Preliminary Analysis of 3DCRT vs IMRT on High Dose Arm of RTOG 0126 Prostate Cancer Trial: *Toxicity Report*

JM Michalski, Y Yan, DW Bruner,
W Bosch, K Winter, JM Galvin,
JP Bahary, GC Morton,
M Parliament, H Sandler

Preliminary Analysis of 3DCRT vs IMRT on High Dose Arm of the RTOG 0126 Prostate Cancer Trial: *Patient Reported Outcomes*

DW Bruner, D Hunt, JM Michalski,
W Bosch, Y Yan, JM Galvin, JP
Bahary, GC Morton, M
Parliament, H Sandler

PROs May Inform Comparative-Effectiveness

Preliminary Analysis of 3DCRT vs IMRT on the High Dose Arm of the RTOG 0126 Prostate Cancer Trial:

Toxicity and Patient Reported Outcomes

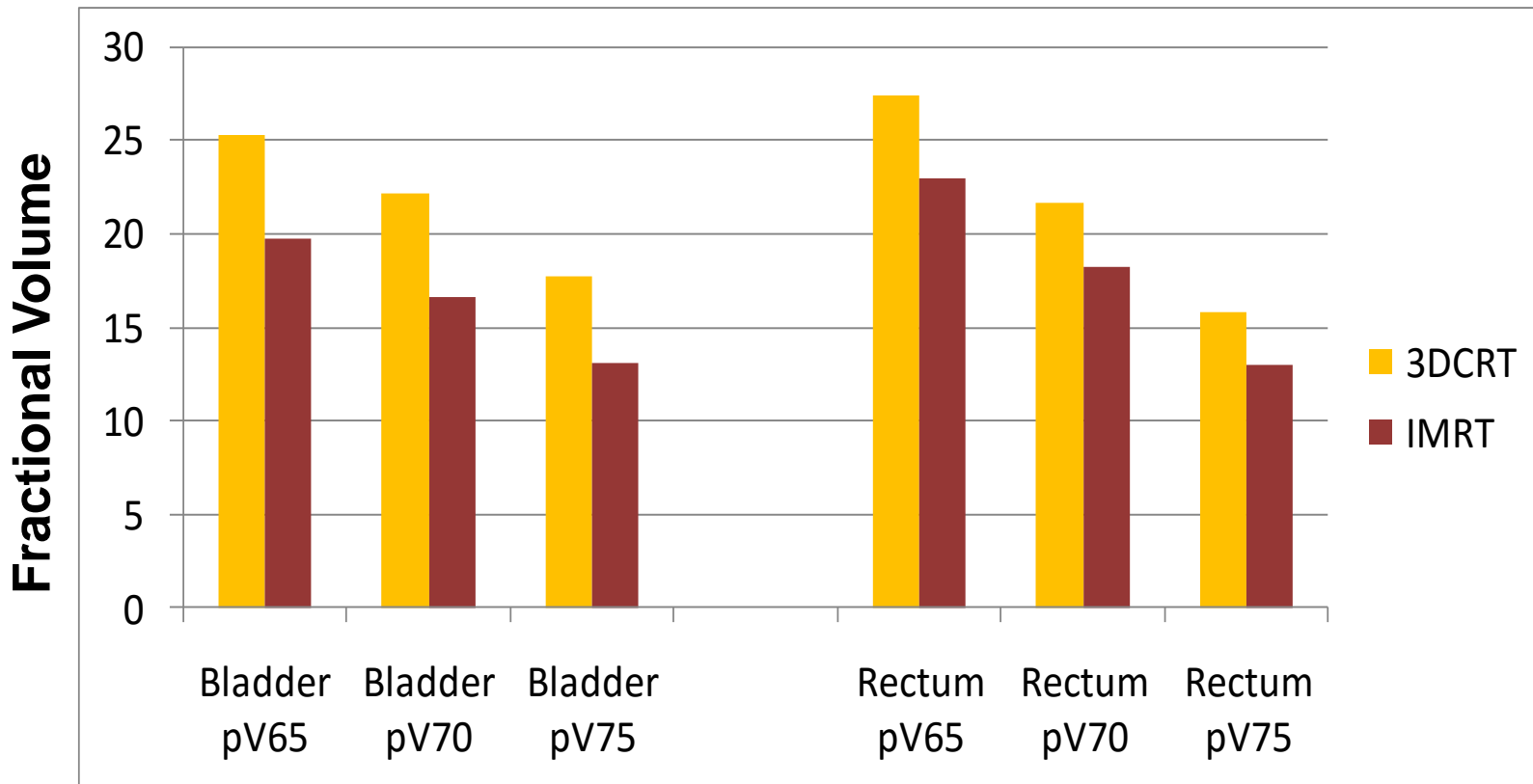
- △ 763 patients randomized to 79.2 Gy arm of RTOG 0126, a trial comparing high to standard dose (70.2 Gy) RT for localized prostate cancer.
- △ Institution declared choice of IMRT or 3DCRT
- △ 499 (65%) patients completed baseline PRO bowel & bladder instrument (Functional Alterations in Changes in Elimination; FACE);
 - Of these, about 2/3 completed PRO instrument at 3, 6, 12, and 24 mos.

CTCAE and PRO Corresponding Items

CTC	Corresponding FACE item (Bruner et al 1994; 2007)
<i>Bowel</i>	
Constipation	I am constipated.
Diarrhea	I have to move my bowels so frequently I am afraid to leave the house
Proctitis	My bowel movements cause me discomfort/pain
Flatulence	I am bothered by gas pains/abdominal aches
Other GI	My bowel habits interfere with my everyday activities
CTC	Corresponding FACE item
<i>Renal/Genitourinary</i>	
Urinary frequency/urgency	I have to urinate so frequently I am afraid to leave the house
Urinary incontinence	I wear a pad, diaper or appliance to prevent urinary "accidents" and I am concerned I may have "dribbling" of my urine
Urinary retention	NONE
Dysuria	I have burning when I urinate.
Bladder/Other GU	My urinary habits interfere with my everyday activities

Dosimetric Comparison

IMRT significantly lowers the high dose volume to bladder and rectum



All differences statistically significant $p < 0.0001$

Results:

FACE	IIEF
No statistically sig. differences between 3DCRT and IMRT	No statistically sig. differences between 3DCRT and IMRT
<ul style="list-style-type: none">▪ at any time point (3, 6, 12, 24 months) for:	<ul style="list-style-type: none">▪ at any time point for overall and 6 or 12 months for any subscale:
<ul style="list-style-type: none">▪ Total FACE score▪ Bladder subscale score▪ Bowel subscales score	<ul style="list-style-type: none">▪ Total IIEF score▪ Five subscale scores<ul style="list-style-type: none"><input type="checkbox"/> Erectile function<input type="checkbox"/> Orgasmic function<input type="checkbox"/> Sexual desire<input type="checkbox"/> Intercourse satisfaction<input type="checkbox"/> Overall satisfaction

PROs May Inform Comparative-Effectiveness

	ACUTE		LATE	
	CTC v 2.0	PRO	RTOG Late Effects	PRO
GU Grade 2+	NS		NS	7% difference
GU Grade 3+	NS		NS	
GI Grade 2+	NS		22% 3DCRT vs 15% IMRT p=0.039	
GI Grade 3+	NS		NS	
Combined GU/GI Grade 2+	15.1% 3DCRT vs 9.7% IMRT p=0.042		NS	
Combined GU/GI Grade 3+	NS		NS	

Bruner DW et al. *Cancer* 121(14): 2015;

Michalski JM, Yan Y, Bruner DW, *Int J Radiat Oncol Biol Phys.* 2013;87(5):2013

Discussion

- Bowel and bladder PROs are congruent with toxicity report of no significant difference in acute GI or GU toxicity.
- Late Gr 2 GI toxicity was sig. at $p=0.04$ but PROs not sig. for late GI or GU
- Sig. differences showing IMRT lowers the high dose volume to bladder and rectum compared to 3DCRT *do not* translate into a patient noticeable effect in bowel and bladder changes...Why?

Adverse Events (CTCAE)	Patient Reported Outcomes (PROs)
Reported as they occur	Collected at discrete time points
Physician assessed	Patient reported
RA interpreted and collected	No external interpretation
Often under-reports pt experience	Picks up more lower grade events
Has NEVER been validated	Validated

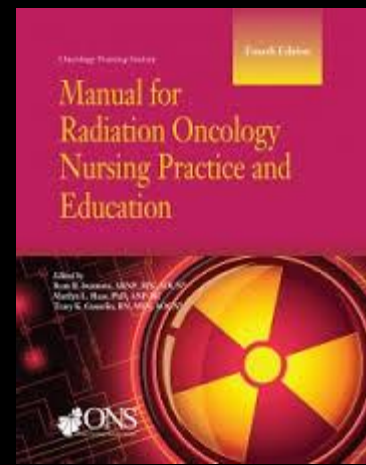


Sustained program of
substantive research





**Research program can
advanced the delivery of
quality patient cancer care**



1991 developed 1st ONS Manual for Radiation Oncology Nursing Practice and Education, which incorporated clinical trial based evidence into the guidelines for practice



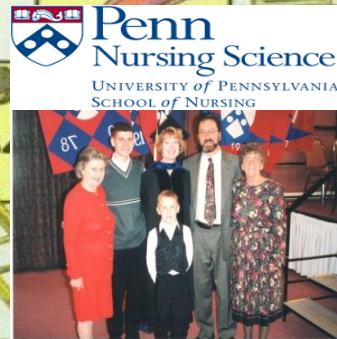
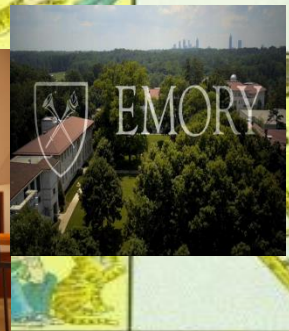
The ONS developed a RT nursing training module building on the Manual for Radiation Oncology Nursing Practice and Education



1990 to 2000 Founder/Chair of Fox Chase Cancer Center Radiation Oncology Conference

- First annual national conference specifically developed to prepare nurses for their role in radiation oncology, incorporating evidence from Dr. Bruner's clinical trials into the evidence based lectures.
- 1,700 nurses from 49 states and 12 countries attended in the first 10 years

Education and Career Ladders and Chutes



“If you limit your actions in life to things that nobody can possibly find fault with, you will not do much!” - Lewis Carroll



“She generally gave herself very good advice, (though she very seldom followed it).”

— Lewis Carroll, Alice's Adventures in Wonderland & Through the Looking-Glass



“One of the deep secrets of life is that all that is really worth the doing is what we do for others.” - Lewis Carroll

Making Informed
Decisions

