Challenges in Prostate Cancer: Why We Are 15 Years Behind Breast Cancer

~ David C. Beyer, MD

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Why Are We 15 Years Behind Breast Cancer

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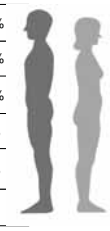
Breast vs Prostate

- Cancer statistics and natural history
- Advocacy
- Research
- Treatment of primary
- Adjuvant hormonal treatments
- Adjuvant chemotherapy treatments

New Cancer Cases

Prostate	234,460	33%
Lung	92,700	13%
Colon & Rectum	72,800	10%
Bladder	44,690	6%
Melanoma	34,260	5%
All Sites	720,280	



Breast	212,920	31%
Lung	81,770	12%
Colon & Rectum	75,810	11%
Uterine	41,200	6%
Non-Hodgkin Lymphoma	28,190	4%
All Sites	679,510	

Jemal, A. et al. CA Cancer J Clin 2006;56:106-130

Cancer Deaths

Lung	90,330	31%
Colon & Rectum	27,870	10%
Prostate	27,350	9%
Pancreas	16,090	6%
Leukemia	12,470	4%
All Sites	291,270	

Lung	72,130	26%
Breast	40,970	15%
Colon & Rectum	27,300	10%
Pancreas	16,210	6%
Ovary	15,310	6%
All Sites	273,560	

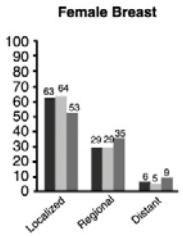
Jemal, A. et al. CA Cancer J Clin 2006;56:106-130

Probability of Developing Invasive Cancers 2000 to 2002

		Birth to 39 (%)	40 to 59 (%)	60 to 69 (%)	70 and Older (%)	Birth to Death (%)
Breast	Female	.5	4.1	3.8	7.1	13.2
Prostate	Male	.01	2.7	7.2	14.5	17.9

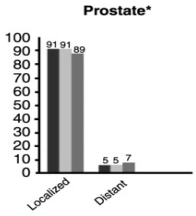
DevCan Software, Probability of Developing or Dying of Cancer Software, Version 6.0.
Statistical Research and Applications Branch, National Cancer Institute, 2005.
hhtp//srab.cancer.gov/devcan.

Breast Cancer at Diagnosis



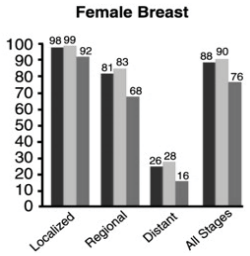
Ries LAG, Eisner MP, Kosary CL. et al.
http://seer.cancer.gov/csr/1975_2002/.

Prostate Cancer at Diagnosis



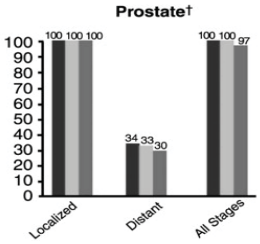
Ries LAG, Eisner MP, Kosary CL. et al.
http://seer.cancer.gov/csr/1975_2002/.

Five-year Survival by Stage: Breast



Ries LAG, Eisner MP, Kosary CL. et al.
http://seer.cancer.gov/csr/1975_2002/.

Five-year Survival: Prostate



Ries LAG, Eisner MP, Kosary CL. et al.
http://seer.cancer.gov/csr/1975_2002/.

Studying Cancer Correlated with:

- **Diet**
  - Fat
  - Fiber
- **BMI**
- **Vitamin A, E, C**
- **Selenium**
- **Alcohol**
- **Caffeine**

Diseases of the Breast, Harris et al, Lippincott-Raven 201-215, 1996

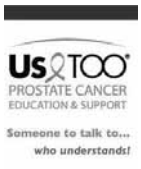
One Day on Google

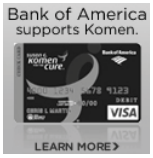
- **Breast cancer:** **7,700,000 hits**
- **Prostate cancer:** **12,000,000 hits**

- **Komen:** **42,800,000 hits**
- **Us Too International:** **204,000,000 hits**

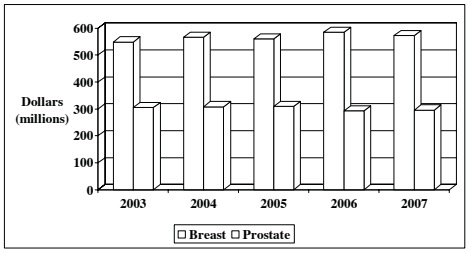
Google, accessed October 15, 2009

Funding





NCI Research Funding



http://obf.cancer.gov/financial/historical.htm

Models for Breast Cancer Spread

- **Halsted**
  - Orderly spread
  - + Node instigator of DM
  - RLN barrier to spread
  - Bloodstream of little significance
  - Local/Regional disease
  - Extent of surgery matters
- **Systemic**
  - No orderly pattern
  - + Node indicator of DM
  - RLN ineffective barrier
  - Bloodstream very important to spread
  - System disease
  - Local/Regional therapy secondary

Halsted, John's Hopkins Hosp Bull, 1895 4:297
Fisher, Breast Cancer Res Treat 1981; 1:17

Treatment Issues

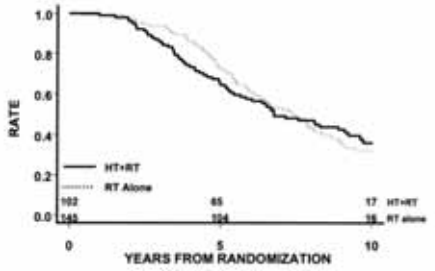
- **Breast**
- **ER/PR receptor assay**
- **Level I evidence**
- **Prostate**
- **Presumed sensitivity**
- **Level I evidence**

Adjuvant Tamoxifen

- Early Breast Cancer Trialists Collaborative Group (EBCTCG)
- 5 years adjuvant therapy
- In receptor positive patients:
  - Odds of recurrence ⇩ 47%
  - Odds of death ⇩ 26%

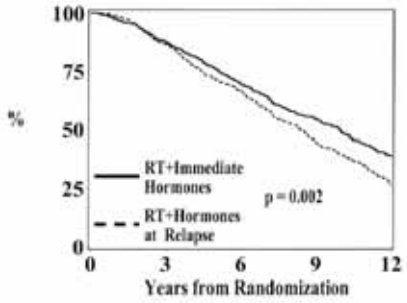
Does Early HT Compromise Late Salvage HT?

Overall Survival RTOG 86-10



Shipley et al, IJROBP, 2002, 54(5):1302-1310

RTOG 85-31 Reduction in Mortality



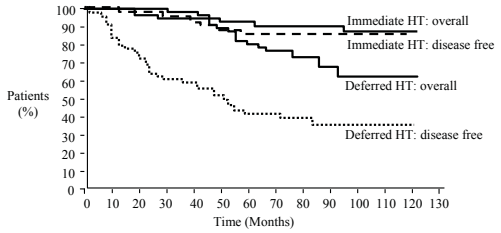
Pilepich et al, IJROBP 61(5) 1283-1290, 2003

Hormones for Prostate Cancer: Short vs Long Term

- RTOG 9202 (+)
  - Locally advanced PSA<150
  - T2 and >25cc, T3, T4
  - RT + Goserelin / Eulexin 2mos. prior and during
  - +/- 2 years Goserelin

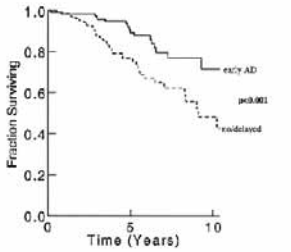
ECOG 7887: Disease-Free and Overall Survival

RP and Pelvic Lymphadenectomy in Node-Positive Patients +/- Hormones



Messing EM, et al. N Engl J Med. 1999;341:1781-1788.

CSS from PSA Failure: Benefit to Early Hormone Therapy



313 Patients

Kestin, Vicini, Martinez; IJROBP, 2004, 60(2):453-462

RTOG 92-02

	Disease Free Survival	bNED	Local Control	Survival	Survival Gleason 8-10
STAD	34%	21%	87%	78%	69%
LTAD *	54%	46%	94%	79%	80%

* ⇑ GI toxicity

Hanks et al, IJROBP 2000 ASTRO

10 Year Update on RTOG 92-02

	Disease Free Survival	bNED	Local Control	Survival
STAD	18%	65%	84%	50%
LTAD	13%	45%	91%	51%
p	0.001	<0.001	0.002	0.25

Hanks et al, IJROBP, 2006, 66(3 Supplement):815 2006

Are Hormones Beneficial in the Era of Dose Escalation?

- **RTOG 0815**
- **Intermediate risk patients**
- **Dose escalation**
  - XRT 79.2 Gy (IGRT ok)
  - XRT 45 Gy + HDR 21 Gy / 2 Fx's
  - XRT 45 Gy + ^{125}I 110 Gy (or ^{103}Pd 100Gy)
- **+/- 6 months TAB**
- **1520 patients**

http://rtog.org/members/protocols/0815/0815.pdf

Available Hormone Options

- **Tamoxifen**
- **Fareston**
- **Arimidex**
- **Aromasin**
- **Femara**
- **Megestrol**
- **Halotestin**
- **Bicalutamide**
- **Leuprolide**
- **Surgical castration**
- **DES**
- **Bicalutamide**
- **Flutamide**
- **Nilandrone**
- **Leuprolide**
- **Goserelin**
- **Degarelix**
- **Surgical castration**

http://www.webmd.com/breast-cancer/hormone-therapy-overview

Hormone Induced Flair

- Worsening pain, bone scan, labs, etc.
- 2-21 days
- 3-20%

Plotkin, et al, JAMA, 1978; 240:2644

Treatment Issues

- **Breast**
- **ER/PR receptor assay**
- **Level I evidence**
- **Hormones**
- **AI's**
- **Prostate**
- **Presumed sensitivity**
- **Level I evidence**
- **LHRH / Antiandrogen**

Treatment Issues

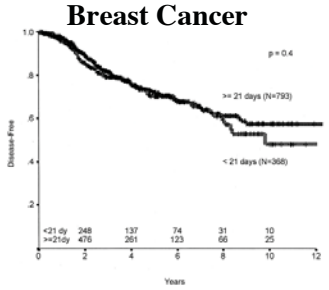
- Breast
- ER/PR receptor assay
- Level I evidence
- Hormones
- AI's
- Chemotherapy

- Prostate
- Presumed sensitivity
- Level I evidence
- LHRH / Antiandrogen
- Chemotherapy (?)

Adjuvant Chemotherapy: Breast

- Standard therapy in 2009 for select patients
- Traditionally started promptly after primary surgical treatment

Timing of Chemotherapy: Breast Cancer



Shannon et al, AJCO 21(20):3792-3797, 2003

Sequencing Chemo/Radiation in Breast Conserving Therapy

- Safe to administer XRT after chemo
- Early (<90 days) chemotherapy reduces local failure

Donato et al. Anticancer Res Mar-Apr 2004;24(2C)"1303-1306

Sequencing of Tamoxifen and Radiation in Breast Cancer

- **1646 women for breast conservation**
- **500 received TAM**
  - 254 up front
  - 241 after XRT
- **No difference in outcomes or toxicity**

Ahn et al. J Clin Oncol 2005;23(1):17-23

Adjuvant Chemotherapy in Prostate Cancer

- **RTOG 0521**
- **High risk**
  - Gleason ≥ 7
  - PSA <150
- **XRT 72-75.6 Gy**
- **2 years LHRH + Antiandrogen**
- **+/- 6 cycles Docetaxel/Prednisone started 28 days after XRT**
- **Reached 600 patient accrual target**

http://rtog.org/members/active.html Accessed Oct 2006

Adjuvant Docetaxel Following RP Phase II RTOG 0621

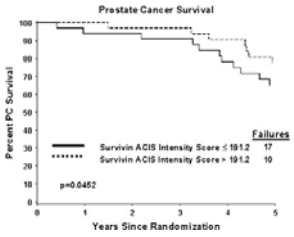
- **Post Prostatectomy**
  - Gleason ≥ 7 and PSA nadir >0.2 ng/ml
  - Gleason ≥ 8 and Stage ≥ T3a (any PSA nadir)
- **Accrual 76 patients**
- **TAB 6 months**
- **XRT 66.6 Gy (at 8 weeks)**
- **Docetaxel 75mg/m^2 q21days x 6 cycles**

Treatment Issues

- **Breast**
- **ER/PR receptor assay**
- **Level I evidence**
- **Hormones**
- **AI's**
- **Chemotherapy**
- **No blood marker**
- **Genetic markers predict sensitivity**

- **Prostate**
- **Presumed sensitivity**
- **Level I evidence**
- **LHRH / Antiandrogen**
- **Chemotherapy (?)**
- **PSA**
- **Limited markers**

Advanced Prostate Cancer Survival by Nuclear Survivin Intensity Score RTOG 8610



Zhang, M. et al. IJROBP. V73(4): 1033-1042, 2009.