Introduction to Prostate Brachytherapy

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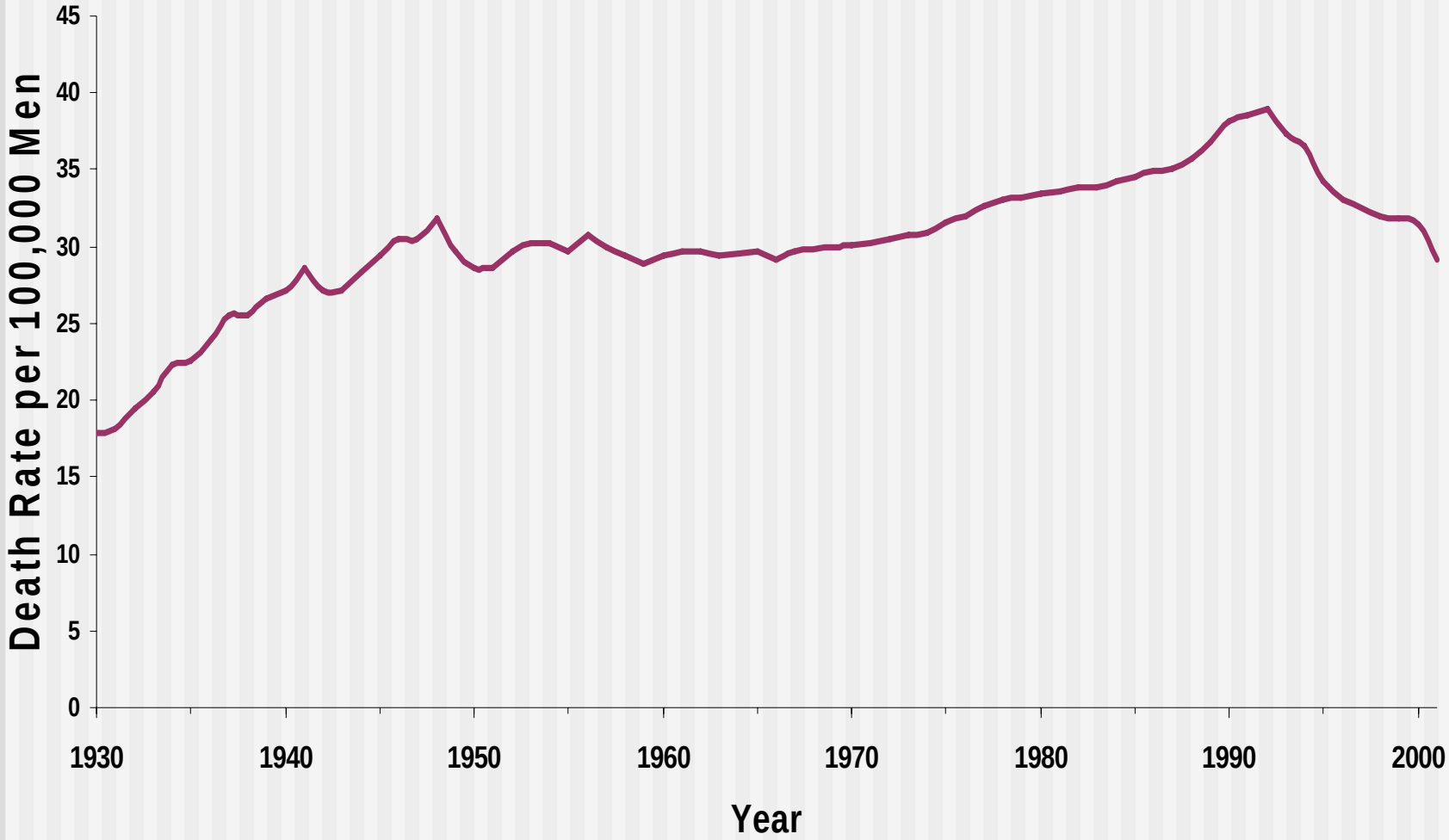
Prostate Cancer Death Rate
(American Cancer Society 2005)



Why the decline in incidence and mortality over the last 10 years?

- Improved treatment isn't the only explanation.
- PSA screening allows diagnosis at earlier stages
  - Earlier stage disease is more curable regardless of improvements in technique or technology
  - Each year screening becomes more prevalent and each year the average patient presents with lower risk
  - Survival comparisons from one time interval to another are not valid because patient characteristics are substantively different.

Prostate cancer clinical staging by the 2002 American Joint Committee on Cancer

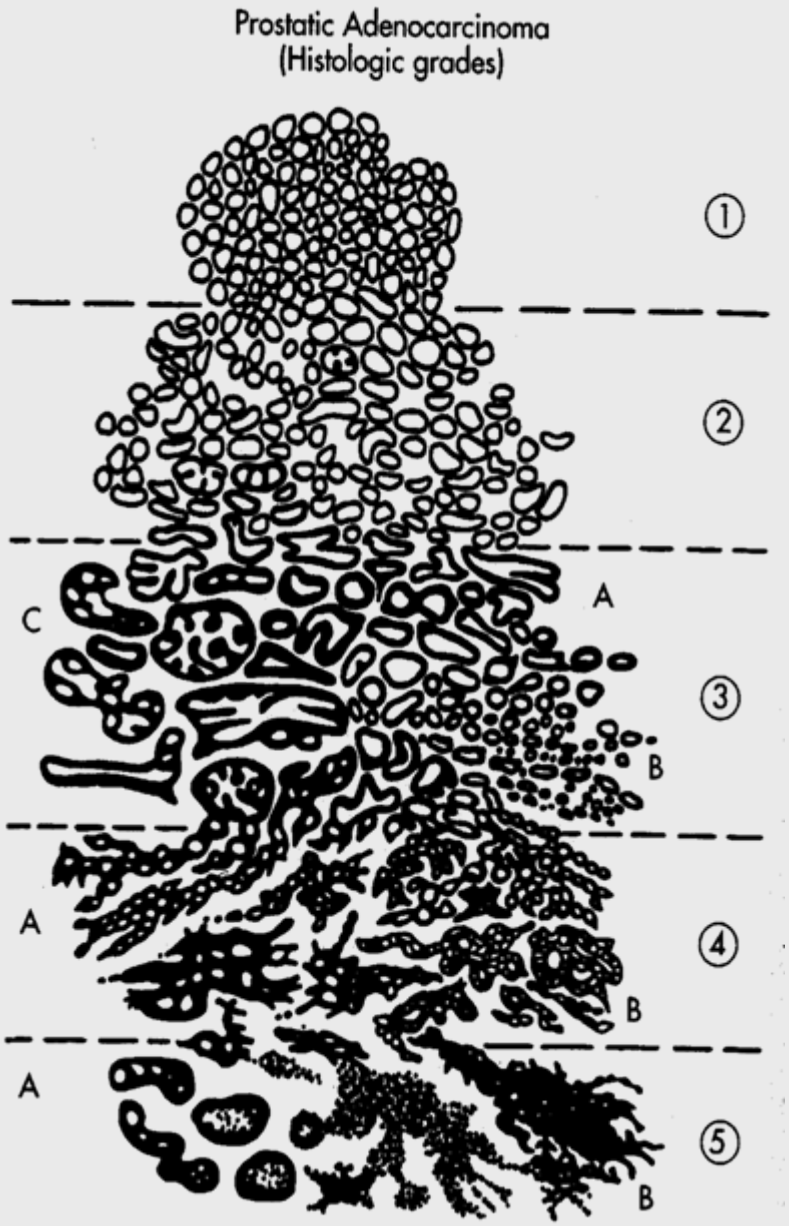
Stage	Description	Substage	Description
cT1	Microscopic disease neither palpable nor visible on TRUS	cT1a	Incidental finding in ≤ 5% of tissue sample
		cT1b	Incidental finding in > 5% of tissue sample
		cT1c	Found on needle biopsy due to ↑ PSA
cT2	Palpable tumor apparently confined within the prostate	cT2a	Involves ≤ half of one lobe of the prostate
		cT2b	Involves > half of one lobe of the prostate
		cT2c	Involves both lobes of the prostate
cT3	Tumor protrudes through the prostate capsule	cT3a	Extracapsular extension of one or both lobes
		cT3b	Seminal vesicle invasion
cT4	Tumor is fixed or invades beyond SV	cT4	Invades bladder neck, muscle, pelvic wall or other

PSA test became widely available in 1988 to measure at ng/mL level

- Demolished false perceptions of treatment efficacy
  - "Is cure possible in those for whom it is necessary — and is cure necessary in those for whom it is possible."
    Willet Whitmore, 1990
- Test has only modest sensitivity and specificity
  - Age specific thresholds: 4.0 ng/mL for age 65 – 70
  - PSA velocity in ng/mL/yr
  - PSA density in ng/mL/cm^3 of prostate
  - Measure PSA isoforms and precursor molecules

Gleason score is pathological measure of tumor aggressiveness

- Based on glandular architecture of stained tissue viewed at medium microscope power
- Well to poorly differentiated patterns are scored from 1 to 5
  - Two most prevalent patterns are added to create a composite score: e.g. grade 3 + grade 4 = GS 7
  - Distribution of scores by national experts:
    GS ≤ 4 is rare, less than 1%
    GS 5 should be about 15% of patients
    GS 6 – 7 should be about 65%
    GS 8 – 10 should be about 19%



Gleason grades

Assign a number corresponding to the most predominant glandular differentiation pattern.

Assign a number to secondary foci of disease.

The sum of the patterns is the Gleason score. If there is no secondary pattern, double the primary number.

A commonly used risk group stratification scheme

Risk Group	Clinical Stage		PSA		Gleason Score
Low (0)	≤ T2b	and	≤ 10	and	≤ 6
Intermediate (1)	> T2b	or	> 10	or	> 6
High (≥ 2)	> T2b	and /or	> 10	and /or	> 6

The purpose of risk group stratification

- Indicates likelihood of organ confined disease
  - Low risk: > 2/3
  - Intermediate: 1/3 to 2/3
  - High risk: < 1/3
  - Use Partin tables for accurate values of organ confinement, extracapsular extension, seminal vesicle and lymph node involvement
- Selects patients for the most appropriate therapy

Other selection criteria

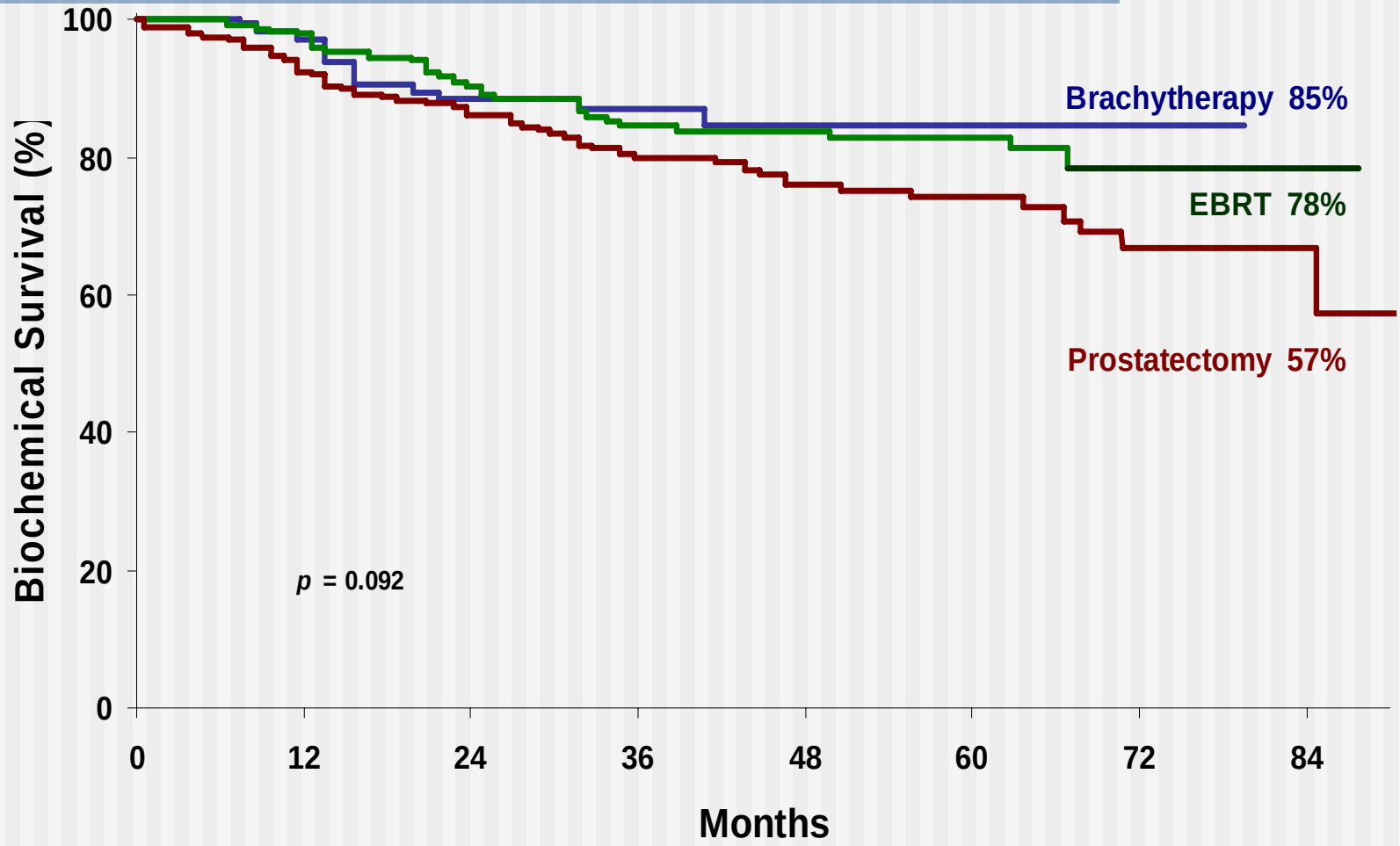
- Quality of life factors scored by questionnaires
  - Urinary function: IPSS
  - Erectile function: IIEF
  - Rectal function: RFAS
- Age — older men are at higher risk of failure
- Co-morbidities — patients should have > 5 years life expectancy
- Anatomy — prostates > 100 cm^3 are difficult and expensive to implant

How to compare survival across modalities?

- There are no randomized trials comparing surgery, brachytherapy, and external beam
  - SPIRIT closed for lack of accrual despite a $5,000 per patient institutional incentive
- Single institution, multi-modality studies
  - Uniform definition of biochemical survival
  - Uniform risk group classification
    - Other factors such as age differ significantly
  - No report has documented that each therapy modality was delivered to meet a standard of quality

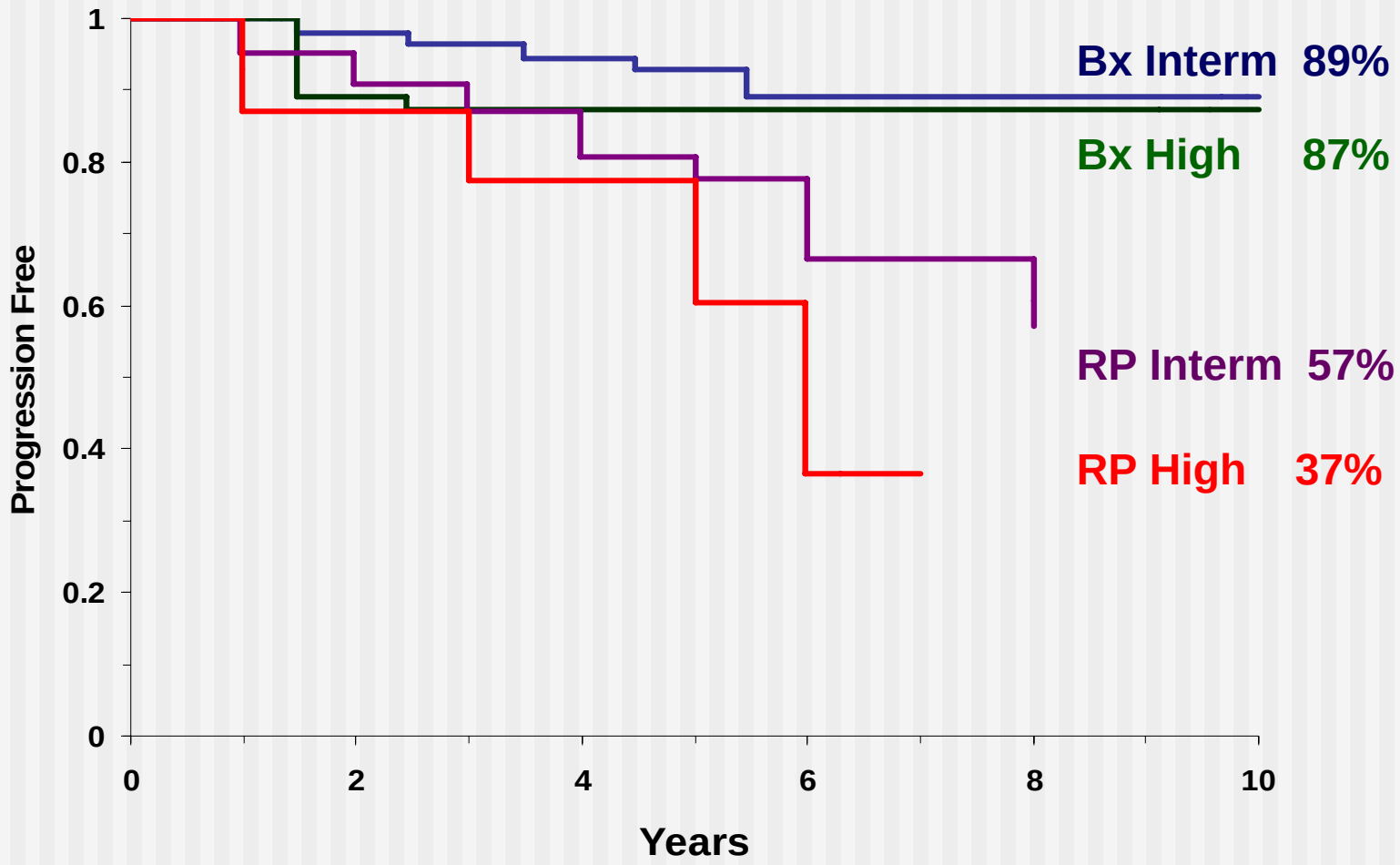
Intermediate risk comparison by treatment modality — Cleveland Clinic

(Ciezki et al. IJROBP 60:1347, 2004)



Single institution comparison by treatment modality

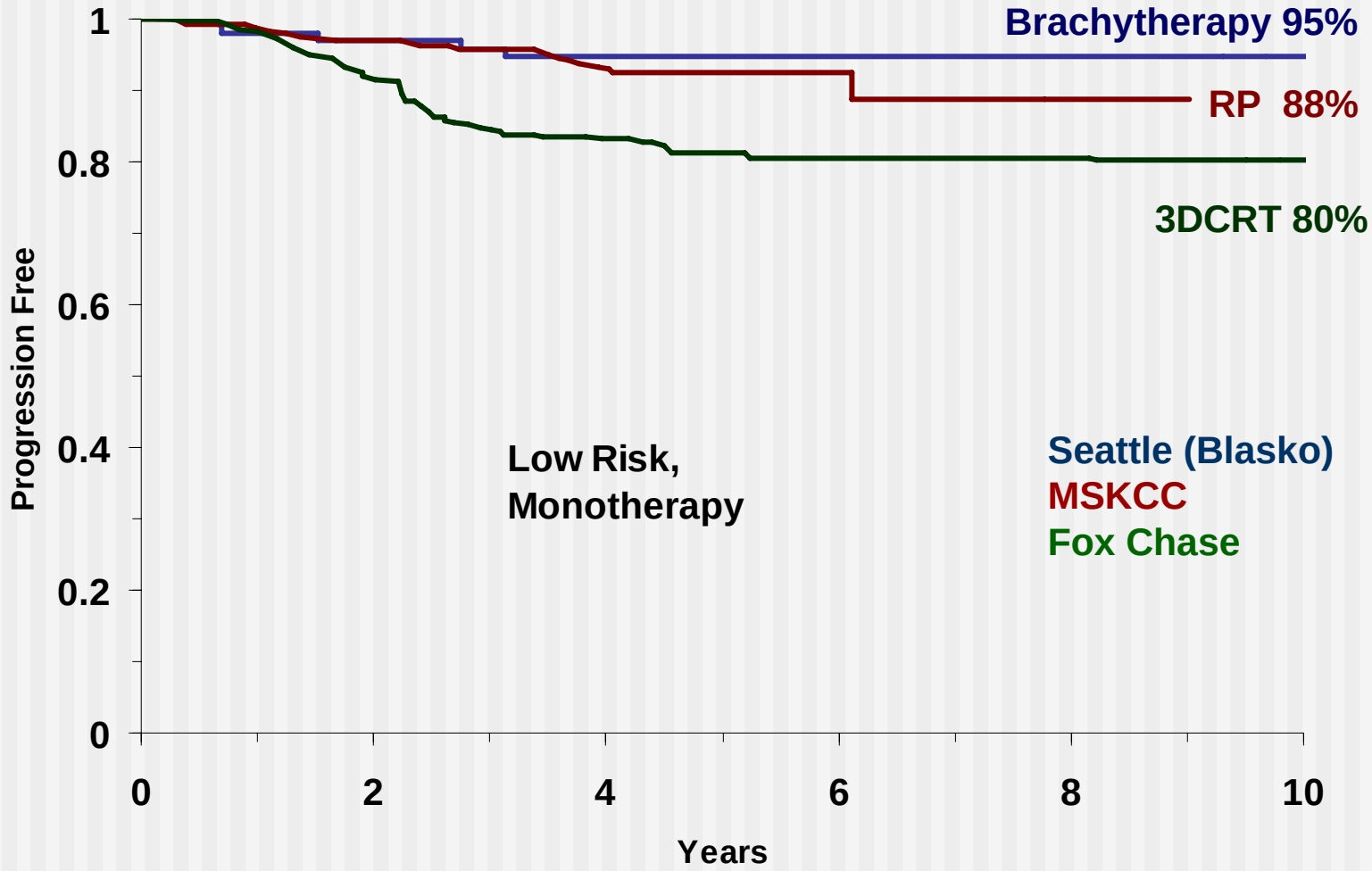
(Sharkey et al. Brachytherapy 4:34-44, 2005)



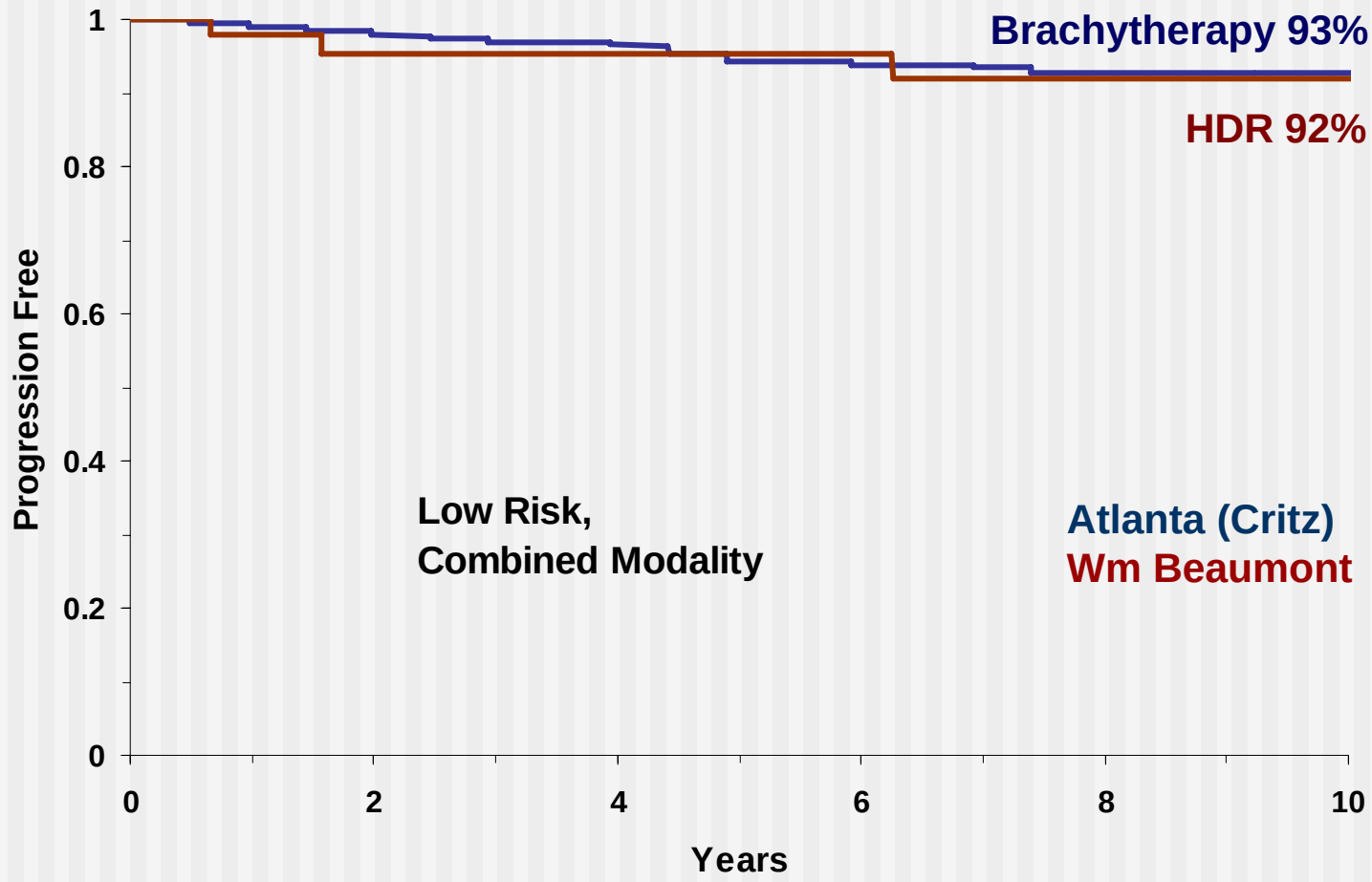
Inter-institution and inter-modality comparisons

- Averaging data across published reports is subject to selection bias
- Search for the best reported results that have been replicated elsewhere
  - Indicates what is achievable or possible
- Patients stratified by standard risk groups
- Treated in the same era
- At least 100 patients per subgroup analyzed
- Minimum 8 years of follow-up
  - ASTRO and nadir definitions of survival become similar at long follow-up

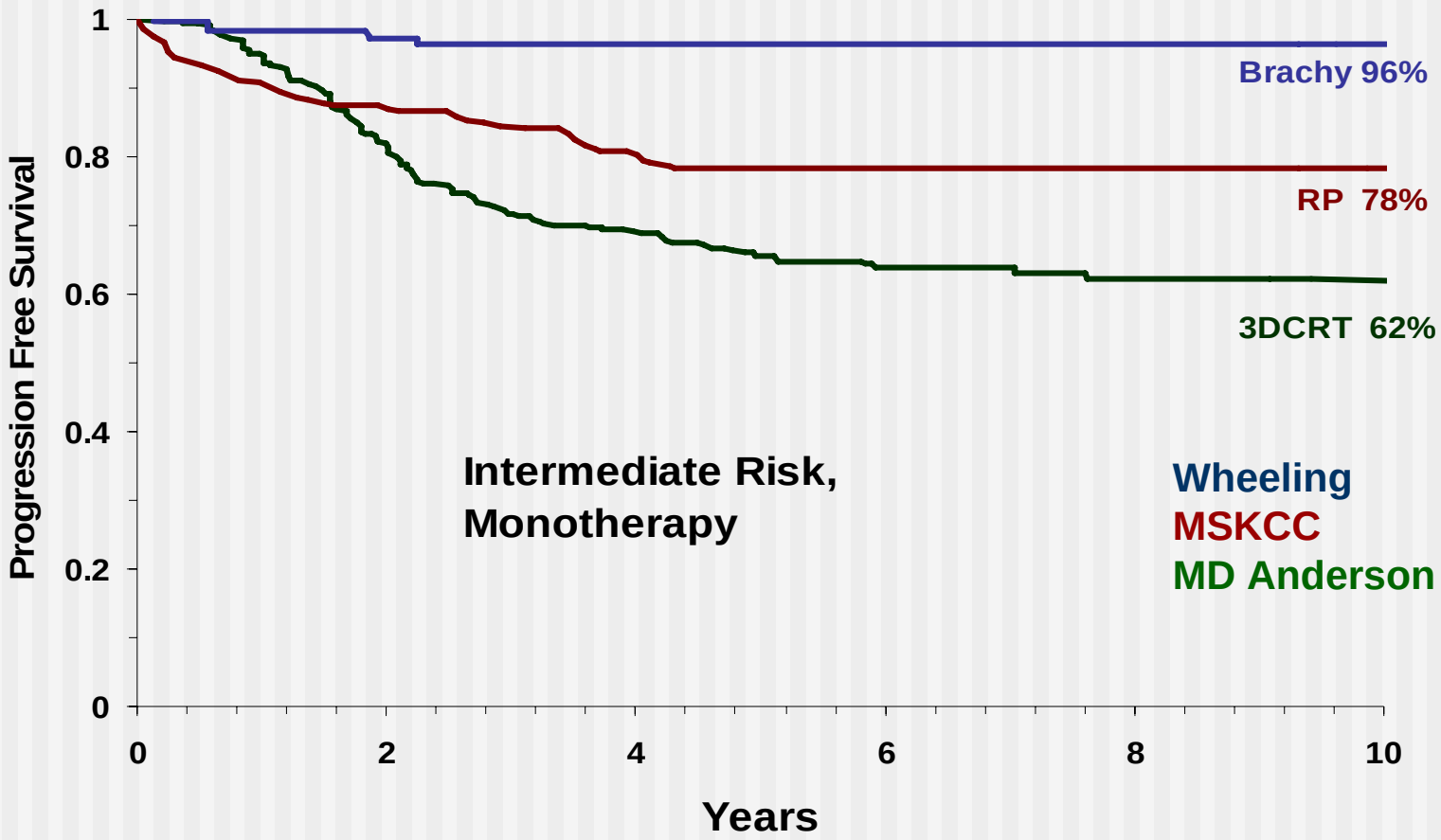
Low risk, monotherapy survival comparison by treatment modality



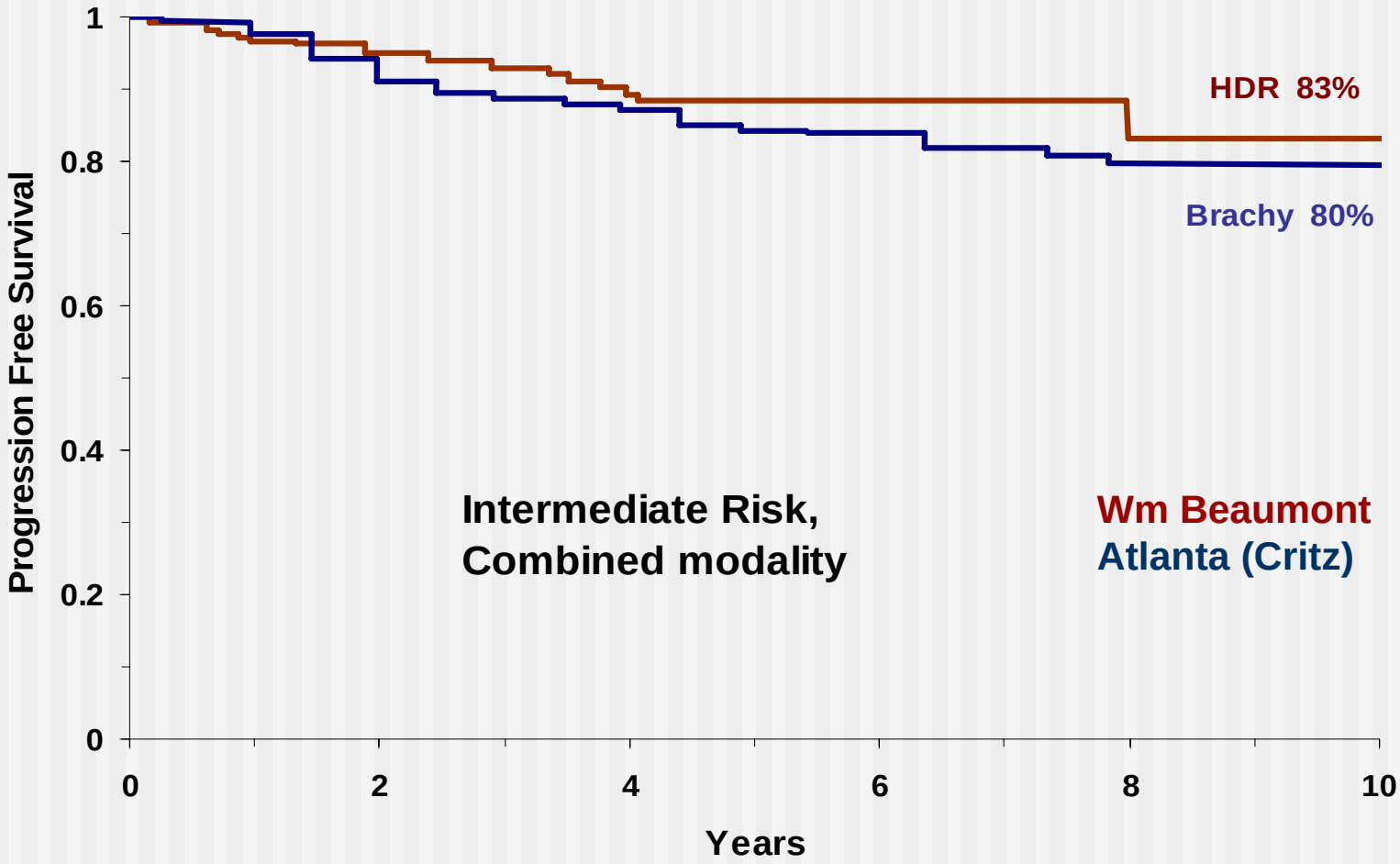
Low risk, LDR and HDR brachytherapy survival comparison with XRT boost



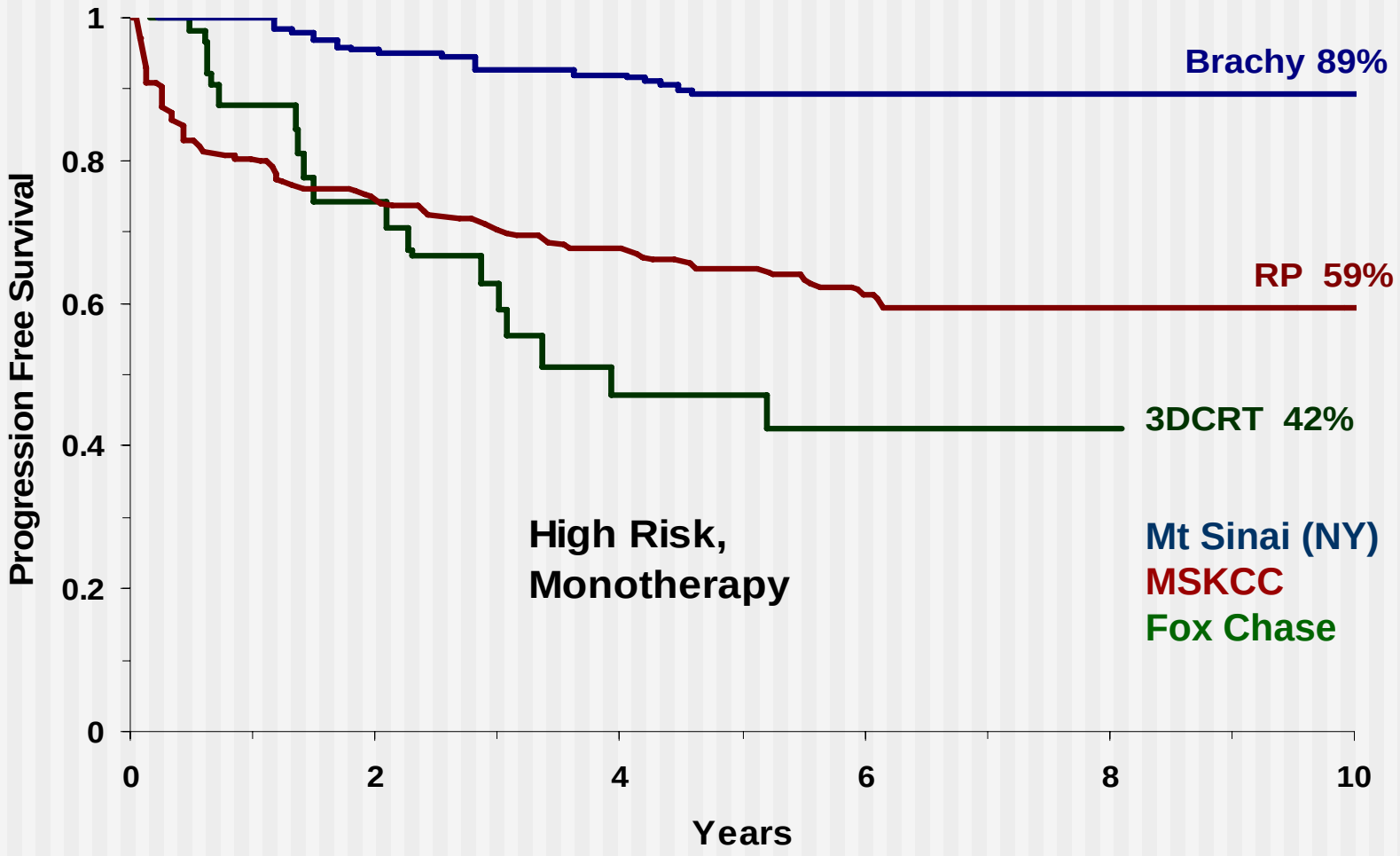
Intermediate risk, monotherapy survival comparison by treatment modality



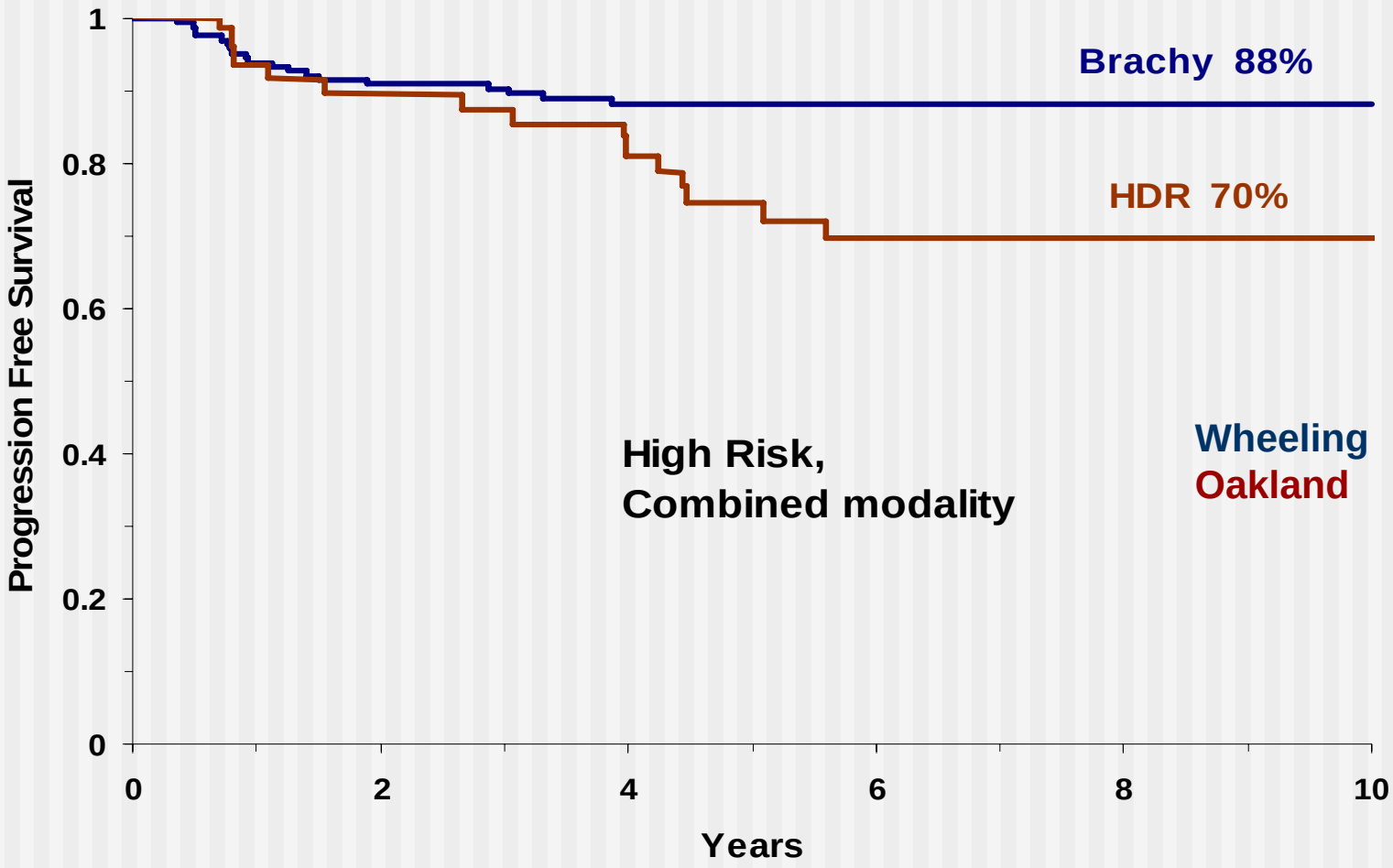
Intermediate risk, LDR and HDR survival comparison combined with XRT boost



High risk, monotherapy survival comparison by treatment modality



High risk, LDR and HDR survival comparison combined with XRT boost



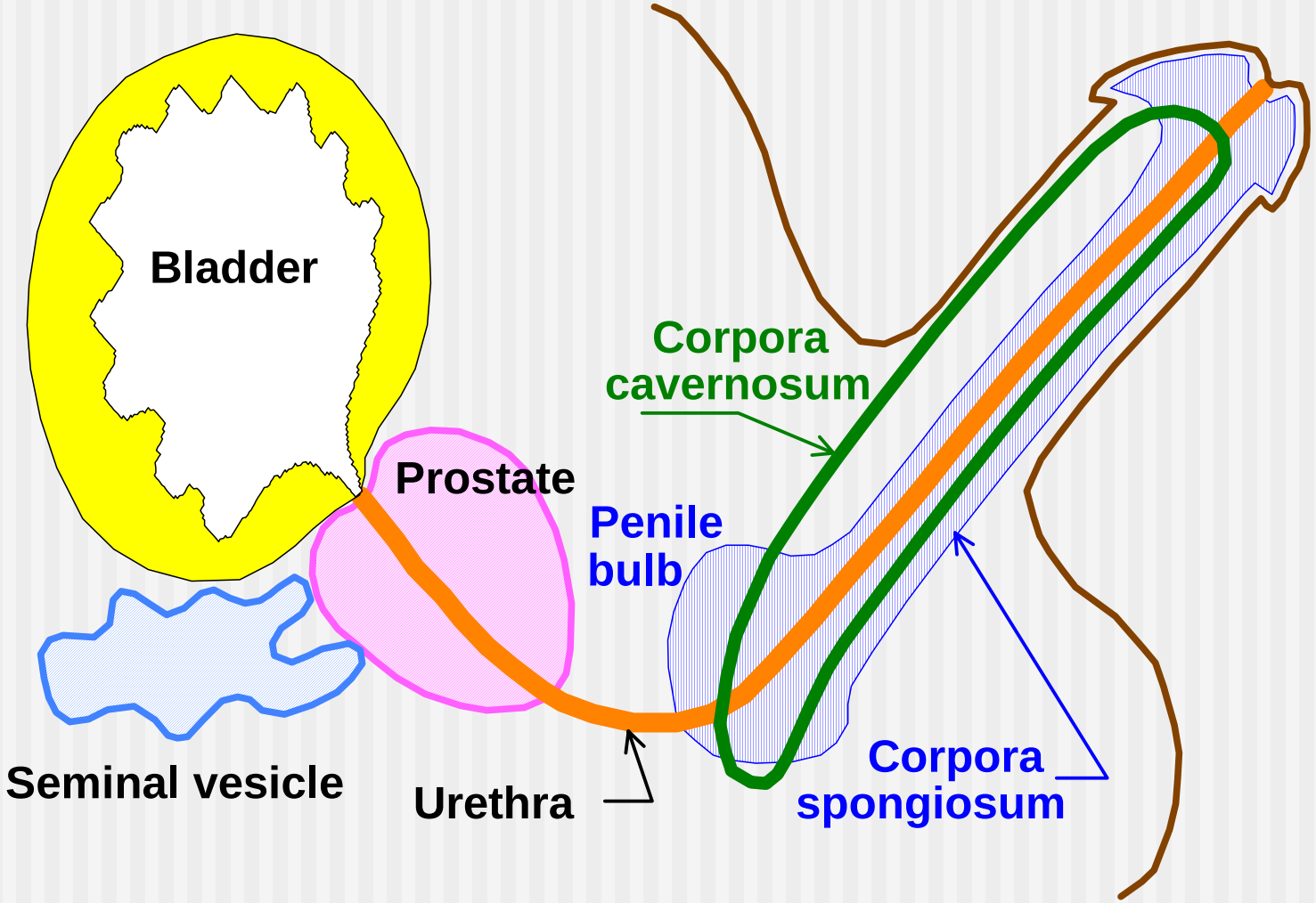
Treatment related morbidity

- Every therapy that cures cancer has morbidity
  - A therapy that claims otherwise has not been sufficiently studied, or the proponents are misinformed or quacks
- Morbidity profiles of brachytherapy, surgery, and 3DCRT differ in frequency and intensity for each effect
  - Comparisons between modalities is beyond the scope of this survey

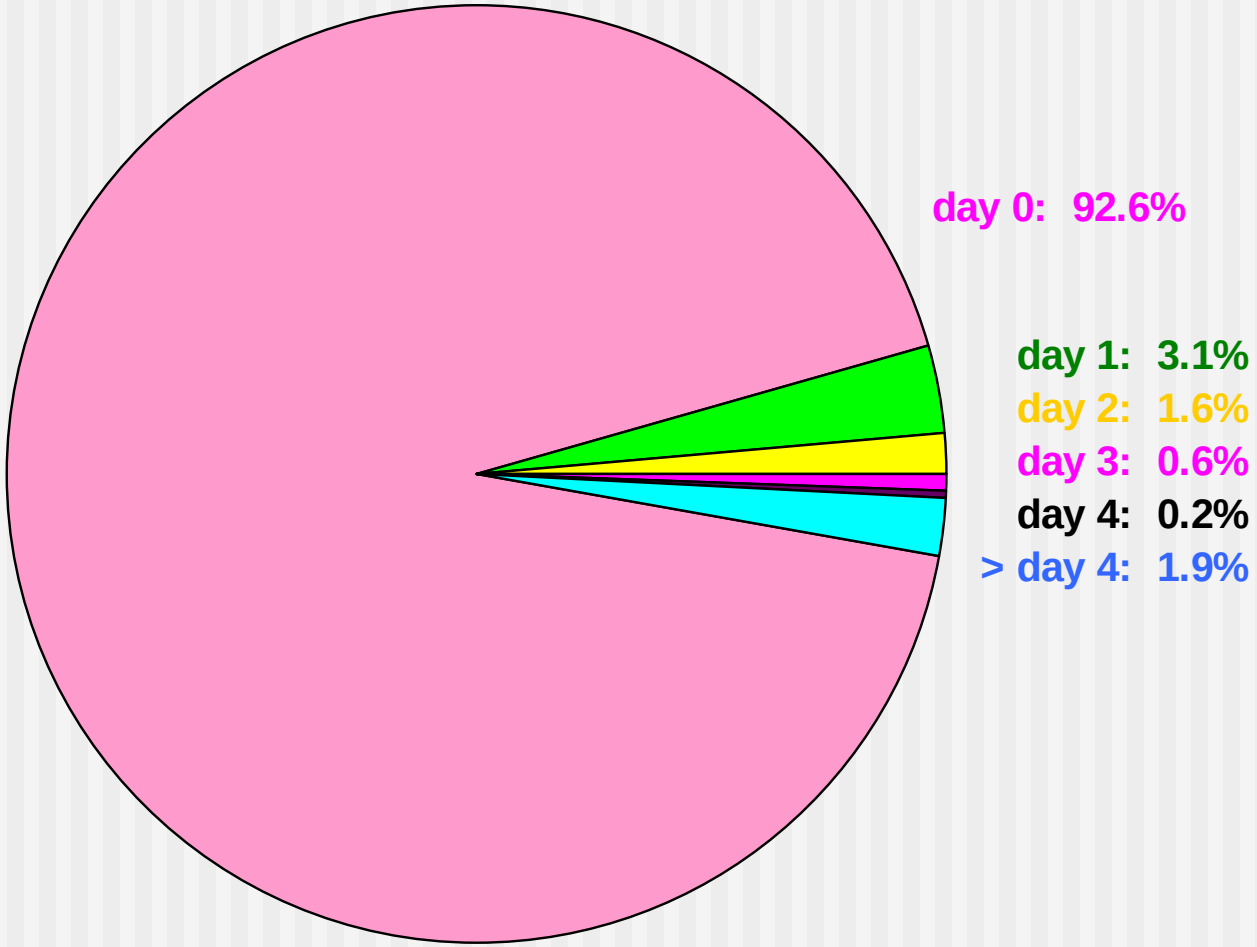
Urinary, rectal and sexual effects

- These side effects appear to follow a critical structure threshold dose response.
  - Below the threshold, the effect is negligible or non-existent
- Structures at risk
  - Prostatic and bulbomembranous urethra
  - Rectal wall
  - Penile bulb

Sagittal schematic of the prostate and nearby structures

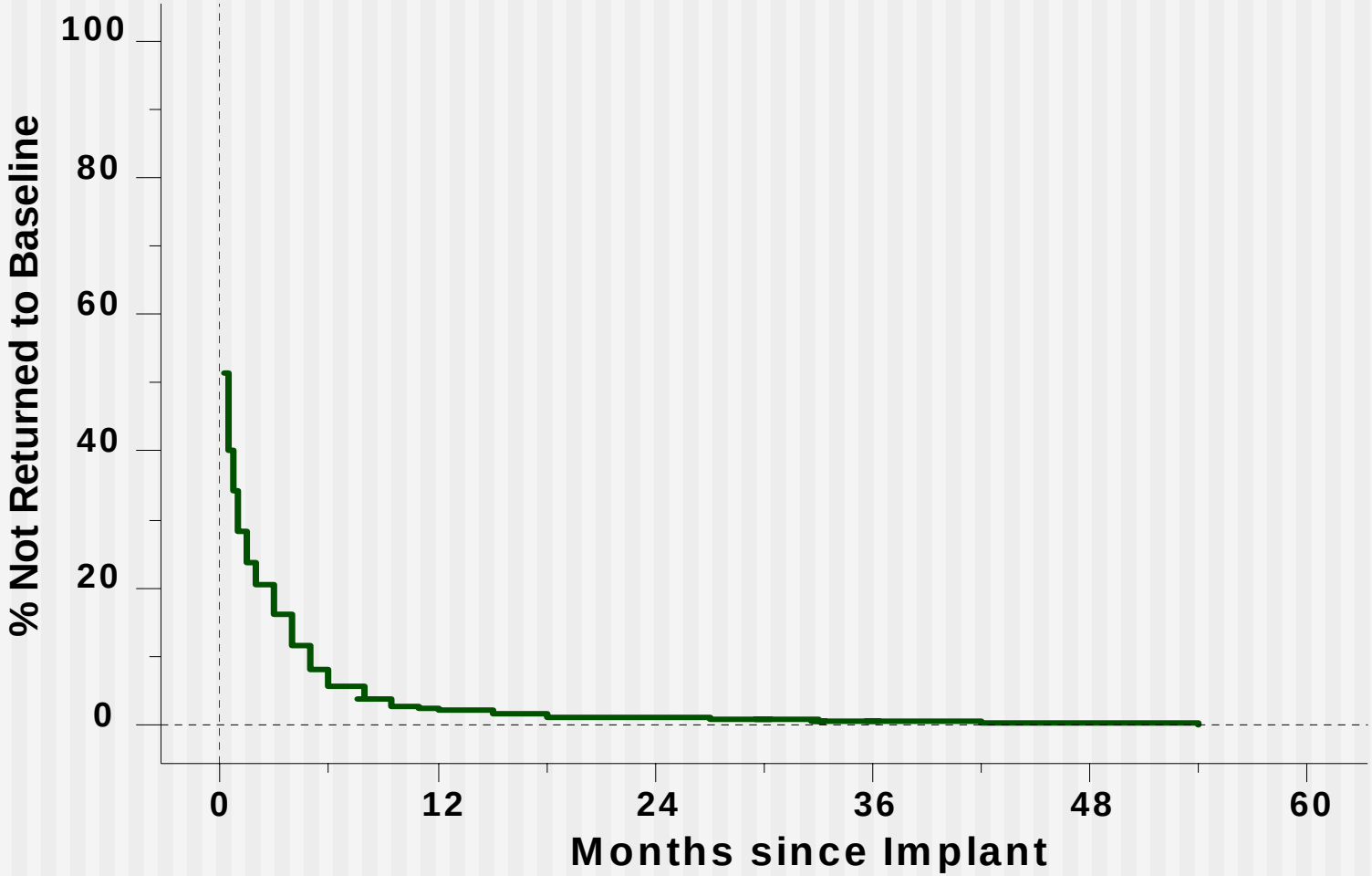


Distribution of postimplant day of urinary catheter removal



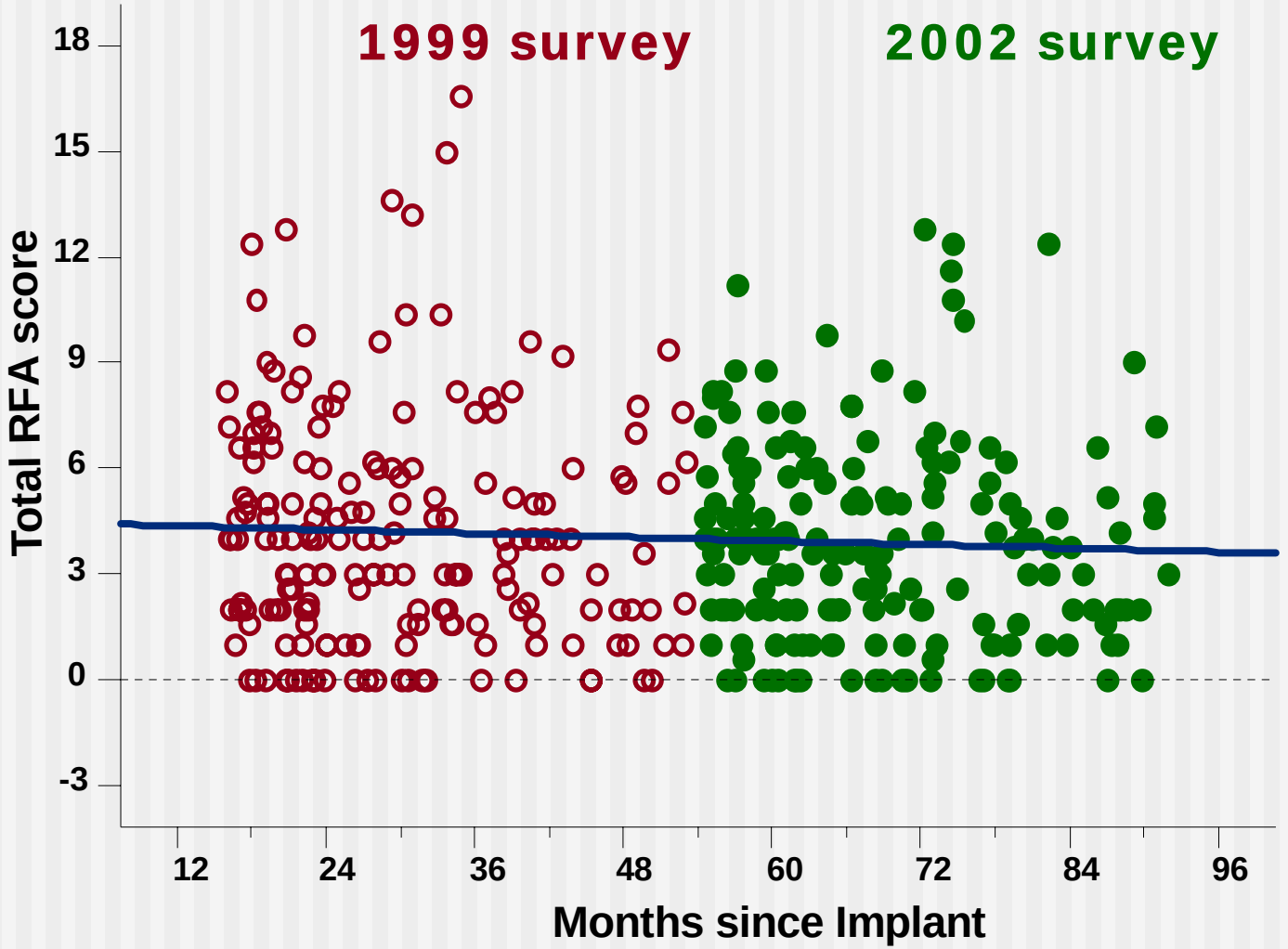
Mean IPSS difference from preimplant baseline
(n = 976)

Kaplan-Meier rate of return to preimplant IPSS baseline *(n = 976)*

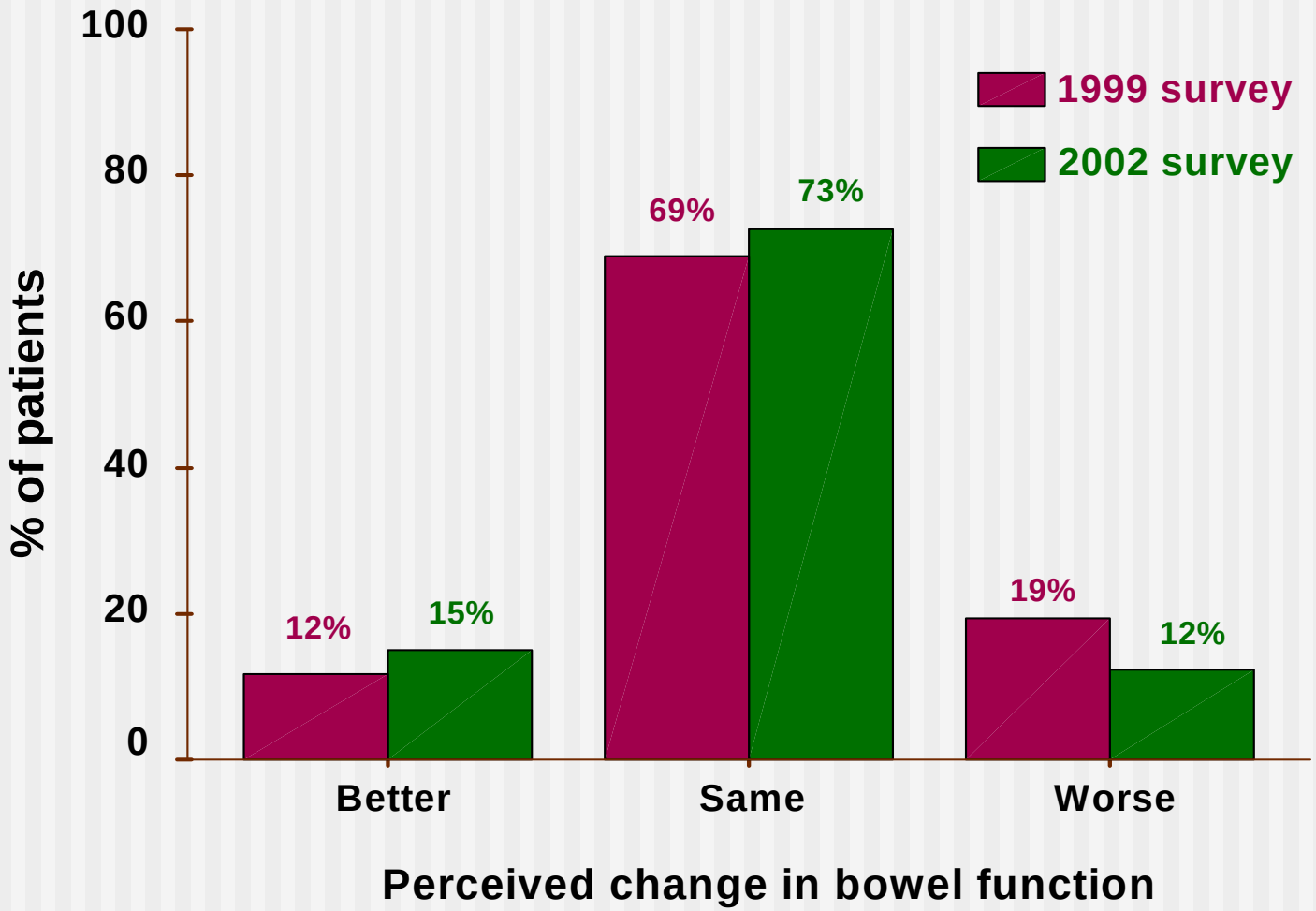


Rectal function assessment score over time

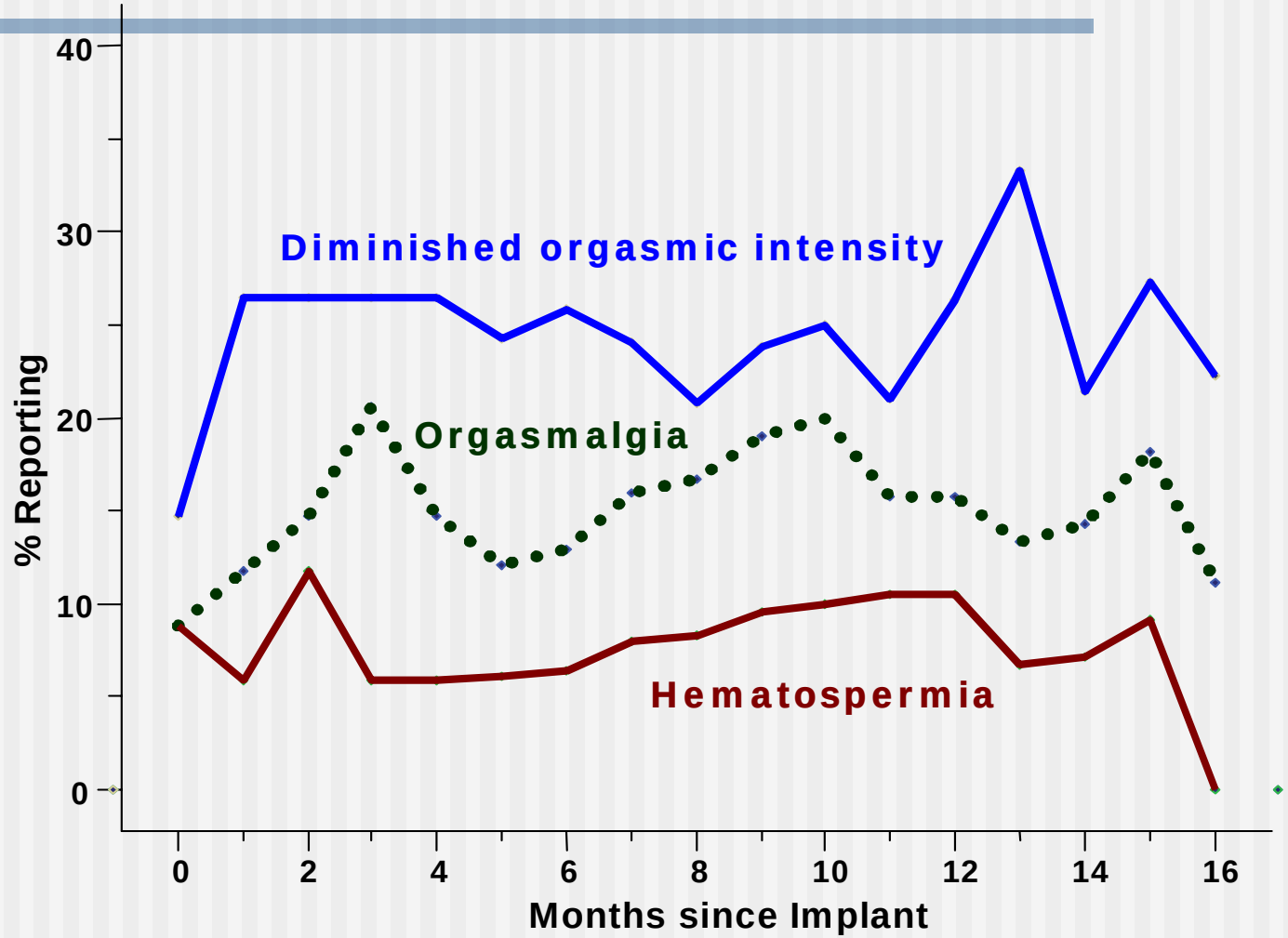
(RFAS scale 0 – 36, preimplant mean = 2.6)



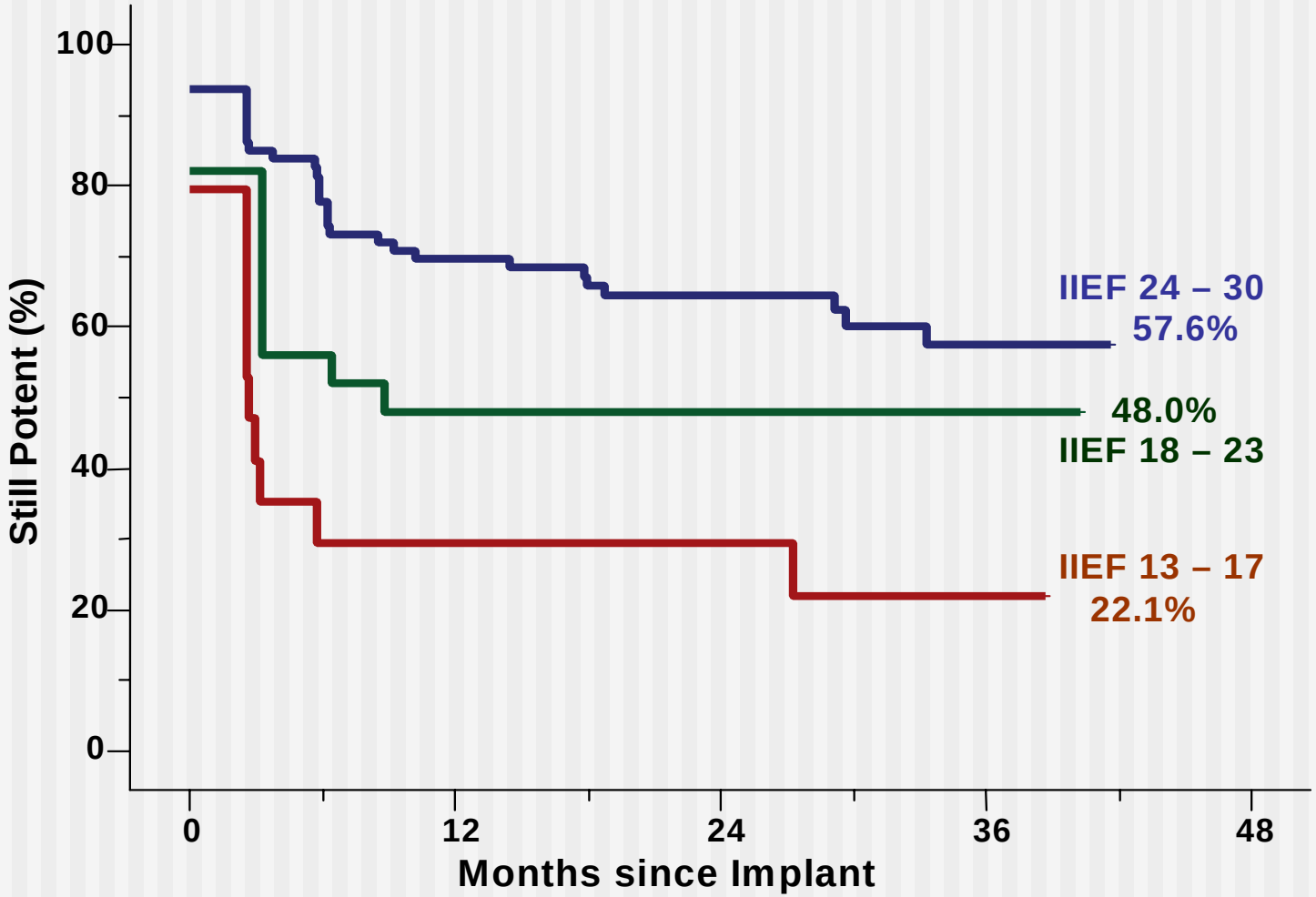
Perceived change in bowel function relative to preimplant status



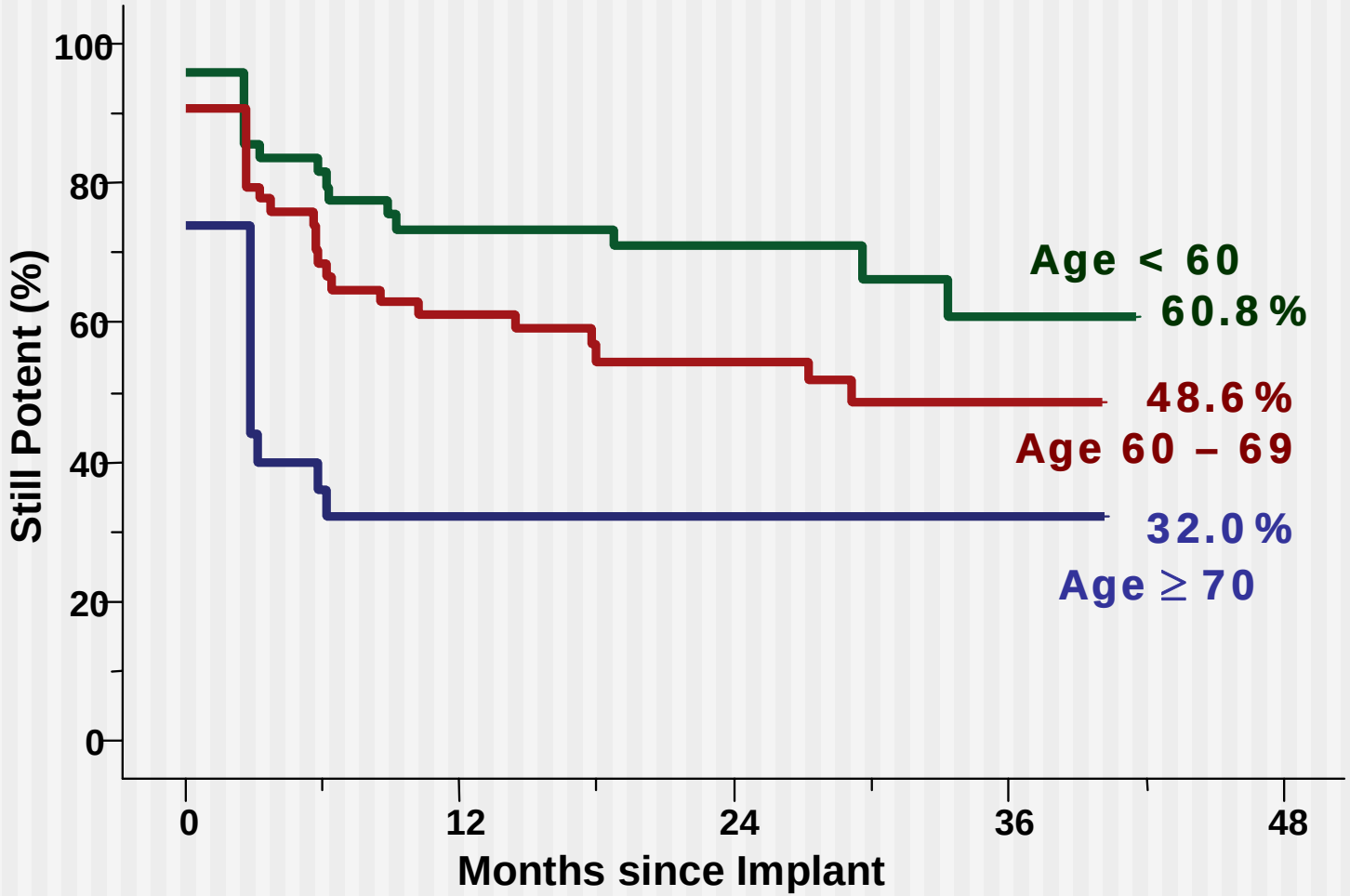
Sexual symptoms reported after brachytherapy (Merrick et al. IJROBP 96:313-319, 2001)



Potency preservation as a function of preimplant IIEF score (Merrick et al.)



Potency preservation as a function of age at implant (Merrick et al.)



Potency preservation stratified by penile bulb D_{50} dose of 30% of prescribed dose