Comparing Treatment Results Of PROSTATE CANCER

Prostate Cancer Results Study Group
Updated January 2017

Prostate Cancer Treatment Research Foundation

Prostate Cancer Results Study

- Problem: Patients, physicians and providers need simple, unbiased data by which to compare the effectiveness of modern prostate cancer treatment methods. The most effective treatments are those in which the patient remains *Prostate Cancer Free*® for their lifetime.

Prostate Cancer Results Study Group

- The Study Group is an assembly of international experts from key treating disciplines:
  - Surgery (RP & Robotic)
  - External Beam Radiation Therapy (EBRT)
  - Brachytherapy (Seeds)
  - High Frequency Ultrasound (HIFU)
  - Proton Therapy (Protons)
  - Cryotherapy (Cryo)
- The purpose of this work is to review all of the current literature on prostate cancer treatment and provide results to patients and their physicians.

Prostate Cancer Results Study Group

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Prostate Cancer Results Study Group

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About This Review Study

- +48,700 prostate articles were published between 2000 and June 2016.
- 1,502 of those articles featured treatment results.
- 223 articles have met PCRSG criteria to be included in this review study.
- Some treatment methods are under-represented due to failure to meet criteria.

About This Review Study

- "Will I be cured?" or "Will my treatment make me cancer free?" are valid patient questions.
- The indicator of being *Prostate Cancer Free*® is a low PSA level which does not rise.
- Five to ten years after treatment, a low PSA level indicates cancer is controlled and there is a high likelihood the cancer will not return.
- Results greater than five years are necessary to be able to compare treatment results.
- Success is defined as PSA at a low level and not rising during the lifetime of a patient "*Prostate Cancer Free*®."

About This Review Study

- After prostate surgery, PSA numbers usually fall rapidly to very low numbers and stay low.
- After radiation, PSA numbers usually come down slower, and may increase briefly, then subsequently fall (this is called a "PSA Bump.")
- These different PSA expectations result in dissimilar ways to review a man's PSA history to judge treatment success.
- A consistent rise in PSA after five years is generally considered a treatment failure.

Abbreviations

Brachy = Seed Implantation (Brachytherapy, either permanent or temporary seeds)

EBRT= External Beam Radiation Therapy (includes IMRT = Intensity Modulated Radiation Therapy)

RP = Standard Open Radical Prostatectomy

Robot RP = Robotic Radical Prostatectomy

HIFU = High Intensity Focused Ultrasound

Cryo= Cryotherapy

Protons = form of External Radiation using Protons

ADT= Hormone Therapy

Article Review Process

- The expert panel agreed unanimously on the criteria an article has to meet to be accepted for comparison purposes.
- Every Prostate Cancer article written between 2000 and June 2016 was reviewed. First to determine if it was a treatment article, and secondly if it met the expert panel's inclusion criteria.
- The results of the accepted treatment articles were plotted together according to each risk group's "*Prostate Cancer Free®*" status (in the professional literature this is known as PSA Progression Free status, meaning no evidence of a rising PSA.)

Article Review Process

- All article evaluations and graph plottings are reviewed by the Article Review Committee and then submitted to the Expert Panel for confirmation prior to all study updates.
- All data recipients, including patients and physicians, are invited to critique the data and submit articles for the PCRSG review process.

Criteria for Inclusion of Article*

1. Articles must be published in a Major Medical Journal.
2. Patients should be separated into Low-, Intermediate-, and High-Risk Groups.
3. Success must be determined by PSA analysis.
4. All major treatment types considered: Seeds (Brachy), Surgery (Standard or Robotic), EBRT (including IMRT), HIFU (High Intensity Frequency Ultrasound), CRYO (Cryotherapy), Protons, HDR (High dose Rate Brachytherapy)

* Expert panel consensus

Criteria for Inclusion of Article

5. Low-Risk articles a minimum of 100 patients.
6. Intermediate-Risk articles a minimum of 100 patients.
7. High-Risk articles, because of fewer patients, a minimum of 50 patients.
8. Patients need to be followed for a median of 5 years.

For additional criteria information contact: l.grimm@pctrf.org

% Articles Meeting Criteria by Treatment

RP	EBRT/ IMRT	Cryo	Brachy/ HDR	Robot RP	Proton	HIFU
9%	16%	6%	24.8%	5.1%	20%	12.7%
37/410	68/427	3/50	100/403	5/98	5/20	6/47

Total of 1,502* Treatment Articles. Some articles addressed several treatments and were counted as separate articles for each treatment. *Some articles evaluated other/minor treatments that are not listed here and are therefore not included in these calculations.

How to Interpret the Graphs

- Each Treatment is given a symbol. For example Seed implant alone (Brachytherapy) is given a blue dot.
- Each Symbol is a different article for that treatment. At the website you can put a cursor over the symbol and actually retrieve that article.
- Treatment Success= Percent of men whose PSA numbers indicate a *Prostate Cancer Free*® Status (PSA progression free) at a specific point in time.
- The bottom line indicates the number years the study is out.
- An example, a blue dot positioned at 12 years along the 97% line indicates that, 97% of the patients, treated with seeds alone in low-risk patients at 12 years were free of disease progression and were *Prostate Cancer Free*®.

How to Interpret the Graphs

- The colored ellipses  outline the results of multiple articles in the same treatment. These were created by our statisticians using standard statistical methods.
- These ellipses demonstrate 2 things:
  - 1. dividing the ellipses in half  will give you the average result of the treatment.
  - 2. The direction of the ellipse will give you an idea of the long term success. A downward direction of the ellipse  indicates that some patients are failing over time.
  - Ideally, if a treatment reaches a point where no or few patients fail, the ellipse pattern will look like this. 
  - There are interactive versions of the graphs on the website: www.pctrf.org/comparing-treatments/ You can choose which treatments and ellipses to view by checking and un-checking the boxes in the key on the right.

How to Interpret the Graphs

- Ellipses are not available for all treatments. They can only be done if there are 4 or more accepted studies within that treatment, so some treatments may not appear on the slides as ellipses only data points.

- In general: Brachytherapy symbols are blue
  EBRT/IMRT symbols are green
  Protons symbols are yellow
  Surgery symbols are red
  Cryotherapy symbols are purple
  HIFU symbols are gray

Treatment Symbols Ledger- for all risk groups graphs

Brachytherapy

- Brachytherapy alone
- Brachytherapy & EBRT
- Brachytherapy, EBRT, & ADT
- HDR (Brachytherapy)
- HDR & ADT (Brachytherapy)

EBRT/IMRT

- EBRT alone
- EBRT & ADT
- Hypo EBRT

Protons

- Protons

Surgery

- RP Surgery
- Robotic Surgery
- RP Surgery & EBRT

Cryotherapy

- Cryotherapy

HIFU

- HIFU

How to Interpret the Results

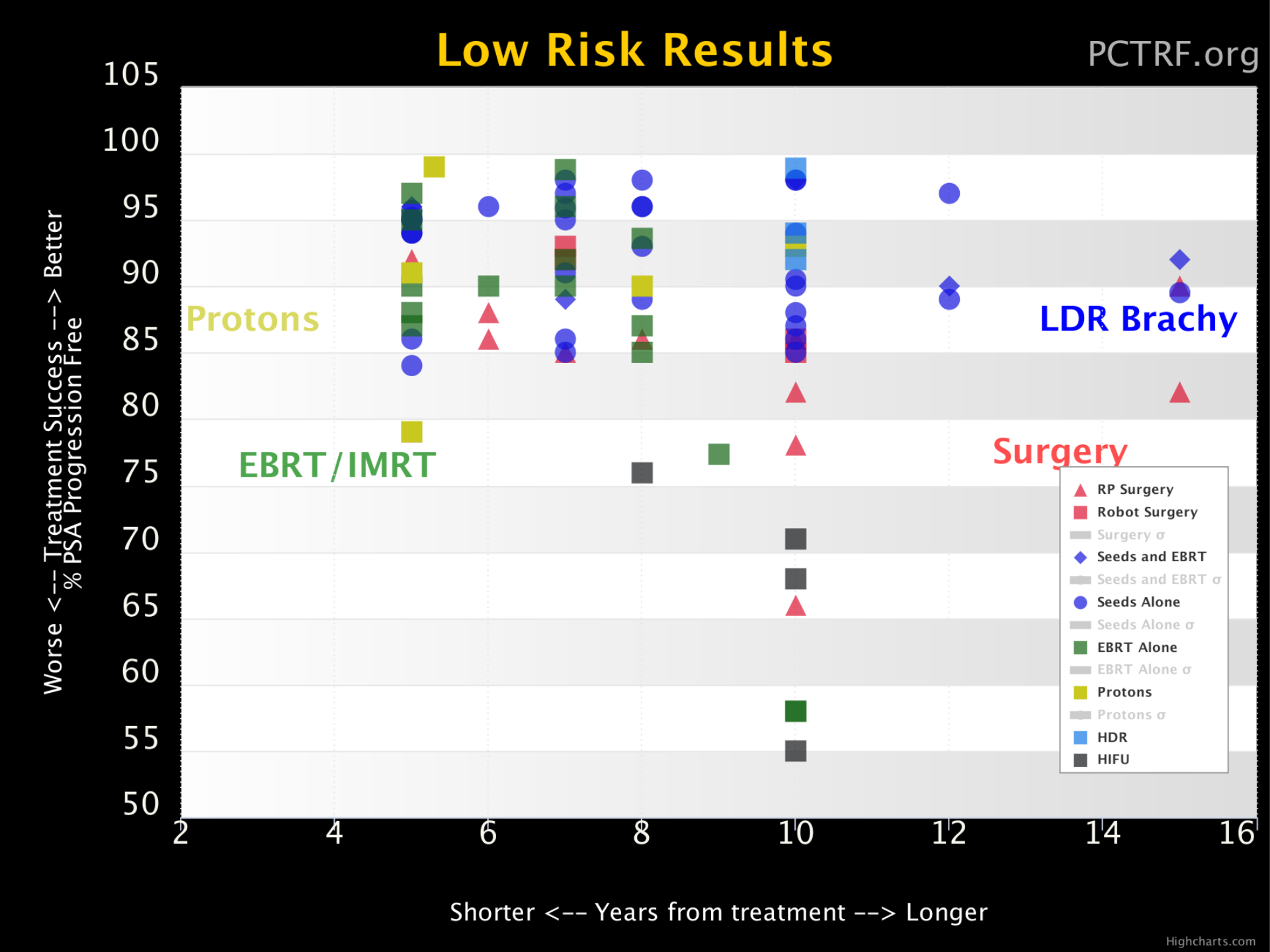
- The Risk groups are defined by a combination of factors. These factors are provided by the diagnosing physician and include the stage of the cancer, the Gleason Score, and PSA level. See slides 20, 23, and 26 for specific definitions for each risk-group.
- First establish your clinical risk group* by looking at the definitions (you can also ask your physician for help in determining you risk group.) Refer only to those slides for your risk group.
- Make your own judgment and then ask a doctor in each discipline (Seeds, External Radiation, Surgery, etc.) to tell you where his/her own peer reviewed published Treatment Success % would fit on this plot.

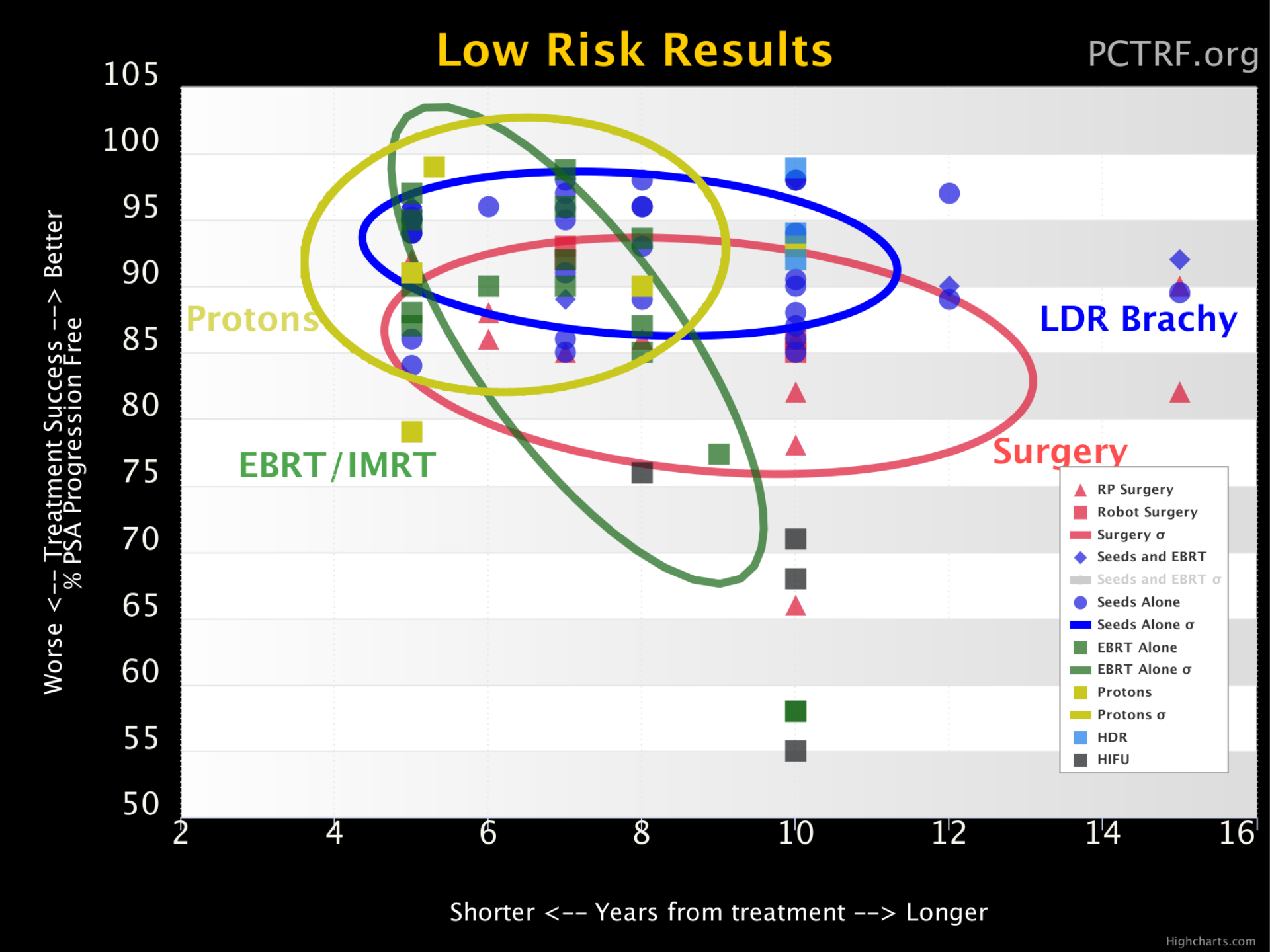
*Next Slide

Low Risk Group Definition

The low-risk group is defined by a combination of factors. These factors are provided by the diagnosing physician and include the stage of the cancer, the Gleason Score, and PSA level. The low-risk group is defined by:

- Clinical Stage: T1 or T2a,b
- Gleason Score $\leq$ 6
- PSA $\leq$ 10 ng/ml


Low Risk Results
PCTRF.org
Worse <-- Treatment Success --> Better
% PSA Progression Free
105
100
95
90
85
80
75
70
65
60
55
50
2
4
6
8
10
12
14
16
Shorter <-- Years from treatment --> Longer
Protons
EBRT/IMRT
LDR Brachy
Surgery
RP Surgery
Robot Surgery
Surgery σ
Seeds and EBRT
Seeds and EBRT σ
Seeds Alone
Seeds Alone σ
EBRT Alone
EBRT Alone σ
Protons
Protons σ
HDR
HIFU
Highcharts.com


Low Risk Results
PCTRF.org
Worse <-- Treatment Success --> Better
% PSA Progression Free
105
100
95
90
85
80
75
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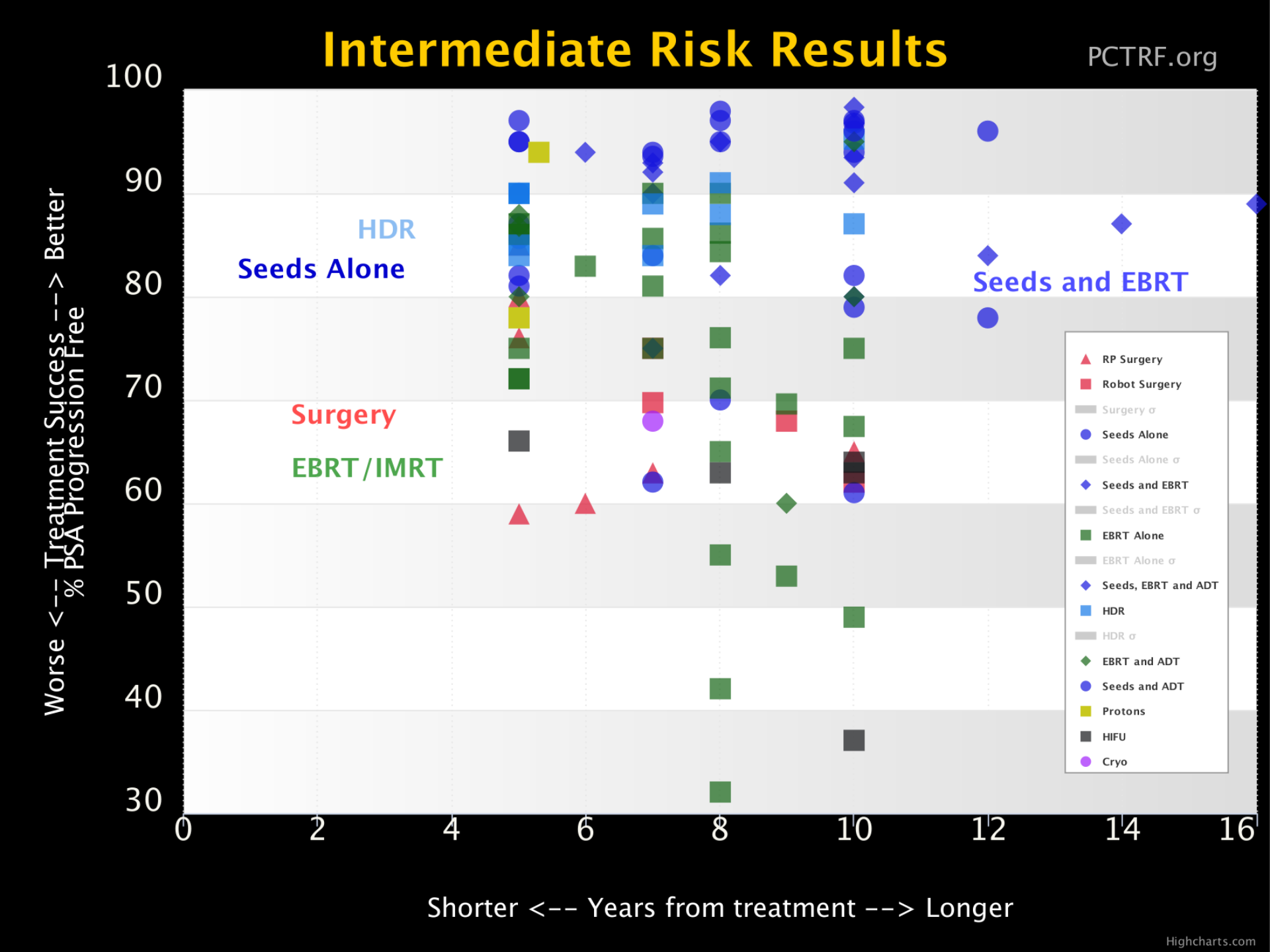
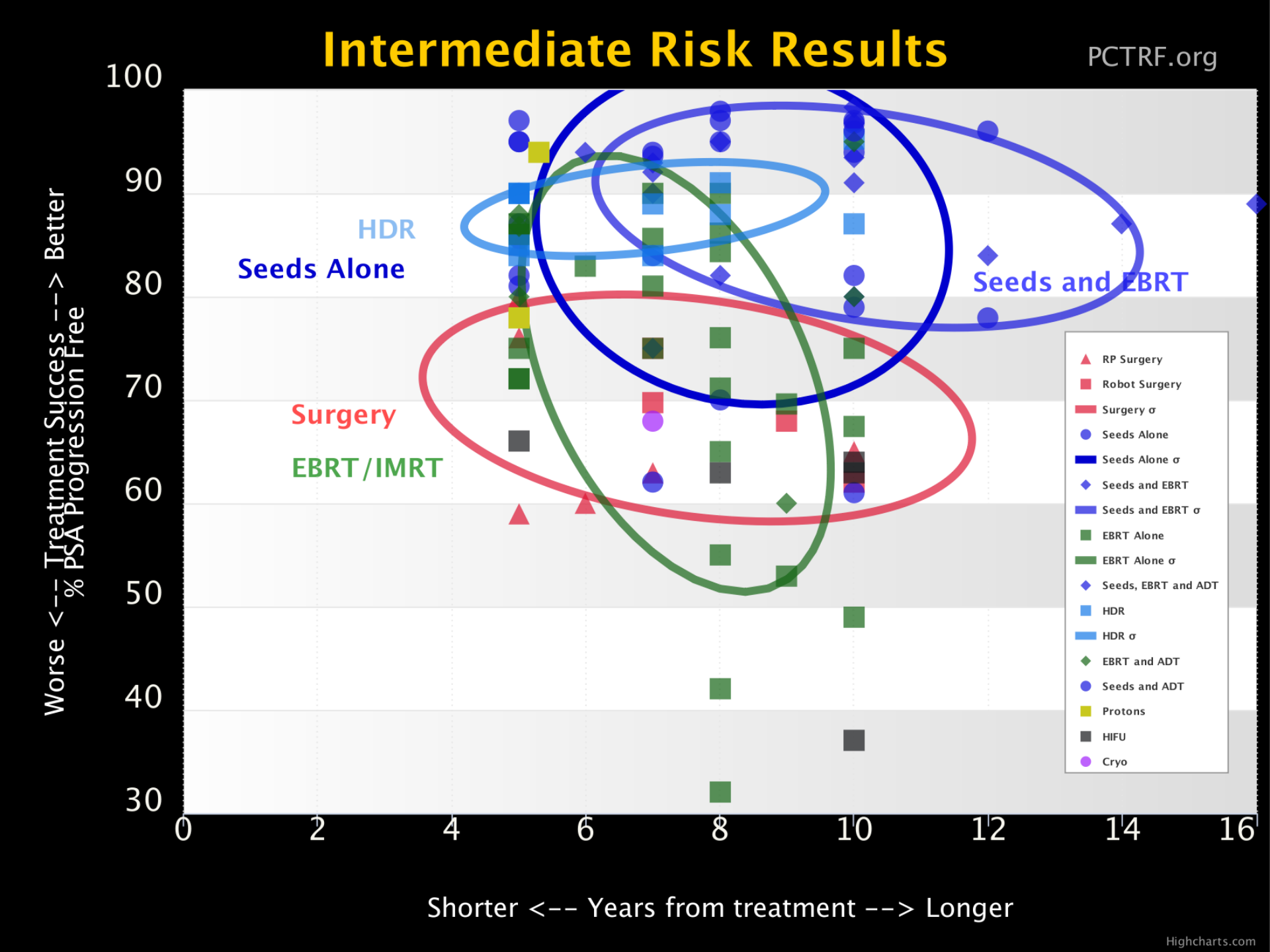
6
8
10
12
14
16
Shorter <-- Years from treatment --> Longer
Protons
LDR Brachy
EBRT/IMRT
Surgery
RP Surgery
Robot Surgery
Surgery σ
Seeds and EBRT
Seeds and EBRT σ
Seeds Alone
Seeds Alone σ
EBRT Alone
EBRT Alone σ
Protons
Protons σ
HDR
HIFU
Highcharts.com

Intermediate Risk Group Definition

The intermediate-risk group is defined by a combination of factors. These factors are provided by the diagnosing physician and include the stage of the cancer, the Gleason Score, and PSA level. The intermediate-risk group has 2 definitions that can be used:

- Zelefsky definition
  - Only 1 factor
    - Clinical Stage T2c
    - Gleason Score ≥ 7
    - PSA > 10 ng/ml
- D'Amico definition
  - PSA 10-20, Gleason Score 7, or Clinical Stage T2b


Intermediate Risk Results
PCTRF.org
Worse <-- Treatment Success --> Better
% PSA Progression Free
100
90
80
70
60
50
40
30
0
2
4
6
8
10
12
14
16
Shorter <-- Years from treatment --> Longer
HDR
Seeds Alone
Seeds and EBRT
Surgery
EBRT/IMRT
RP Surgery
Robot Surgery
Surgery σ
Seeds Alone
Seeds Alone σ
Seeds and EBRT
Seeds and EBRT σ
EBRT Alone
EBRT Alone σ
Seeds, EBRT and ADT
HDR
HDR σ
EBRT and ADT
Seeds and ADT
Protons
HIFU
Cryo
Highcharts.com


Intermediate Risk Results
PCTRF.org
Worse <-- Treatment Success --> Better
% PSA Progression Free
100
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16
Shorter <-- Years from treatment --> Longer
HDR
Seeds Alone
Seeds and EBRT
Surgery
EBRT/IMRT
RP Surgery
Robot Surgery
Surgery σ
Seeds Alone
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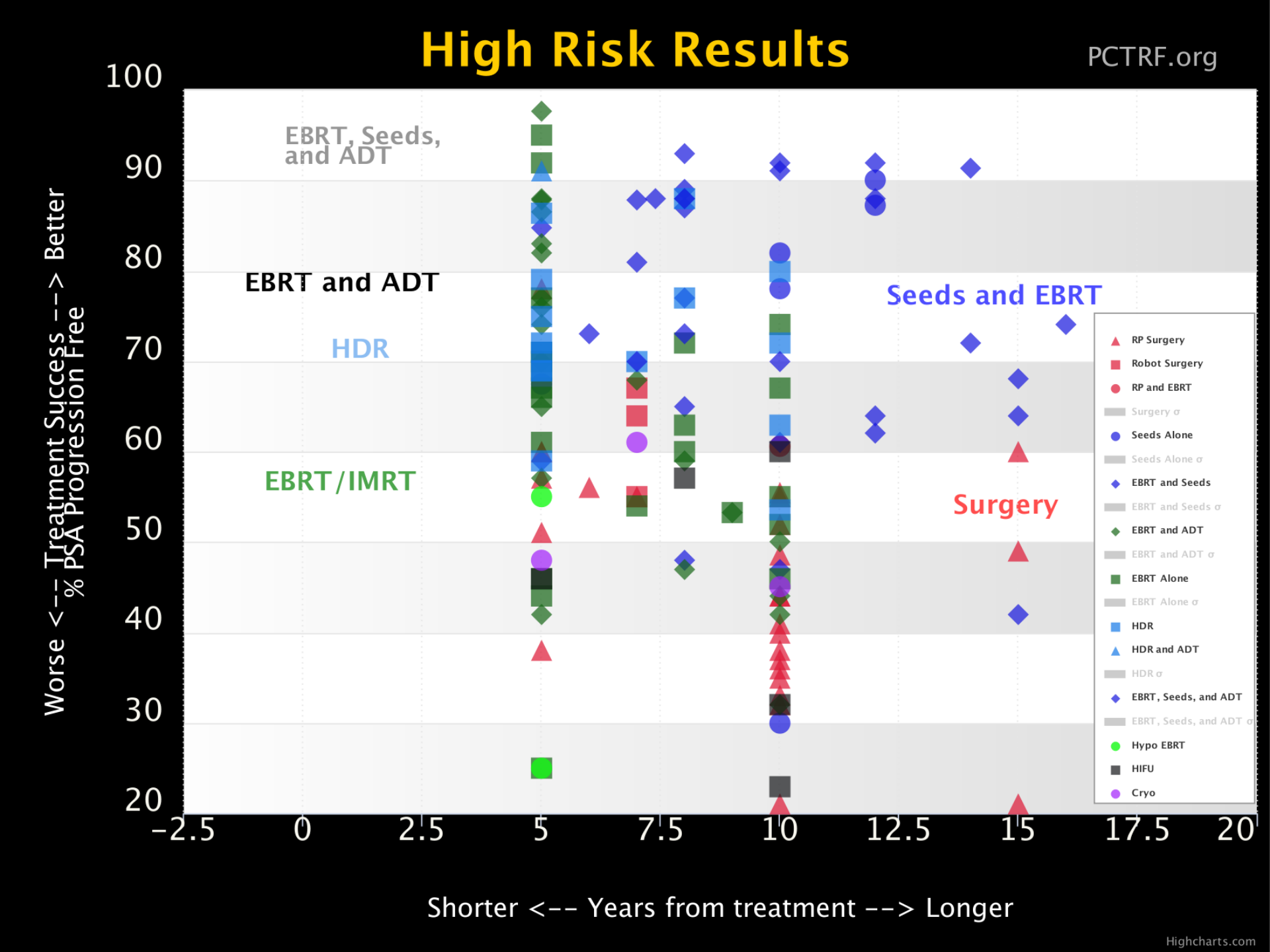
Seeds and EBRT
Seeds and EBRT σ
EBRT Alone
EBRT Alone σ
Seeds, EBRT and ADT
HDR
HDR σ
EBRT and ADT
Seeds and ADT
Protons
HIFU
Cryo
Highcharts.com

High Risk Group Definition

The high-risk group is defined by a combination of factors. These factors are provided by the diagnosing physician and include the stage of the cancer, the Gleason Score, and PSA level. The high-risk group has 2 definitions that can be used:

- Zelefsky definition
  - 2 or more factors
    - Gleason Score > 7
    - PSA 10-20
    - Clinical Stage T1c- T2b
- D'Amico definition
  - Gleason Score 8-10, PSA >20, Clinical Stage ≥T2c


High Risk Results
PCTRF.org
EBRT, Seeds, and ADT
EBRT and ADT
HDR
EBRT/IMRT
Seeds and EBRT
Surgery
Worse <-- Treatment Success --> Better
% PSA Progression Free
Shorter <-- Years from treatment --> Longer
100
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-2.5
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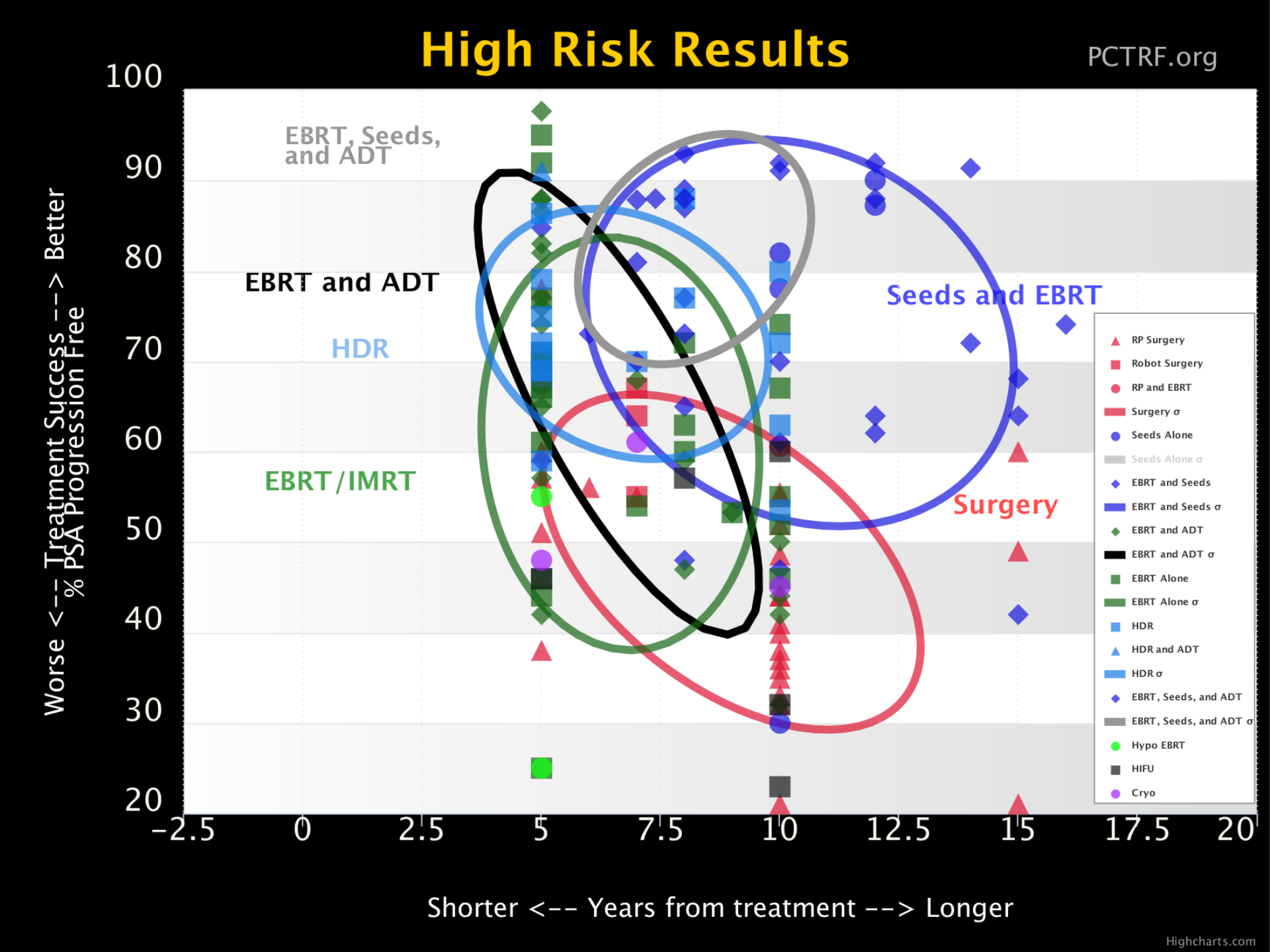
5
7.5
10
12.5
15
17.5
20
RP Surgery
Robot Surgery
RP and EBRT
Surgery σ
Seeds Alone
Seeds Alone σ
EBRT and Seeds
EBRT and Seeds σ
EBRT and ADT
EBRT and ADT σ
EBRT Alone
EBRT Alone σ
HDR
HDR and ADT
HDR σ
EBRT, Seeds, and ADT
EBRT, Seeds, and ADT σ
Hypo EBRT
HIFU
Cryo
Highcharts.com


High Risk Results
PCTRF.org
EBRT, Seeds, and ADT
EBRT and ADT
HDR
EBRT/IMRT
Seeds and EBRT
Surgery
RP Surgery
Robot Surgery
RP and EBRT
Surgery σ
Seeds Alone
Seeds Alone σ
EBRT and Seeds
EBRT and Seeds σ
EBRT and ADT
EBRT and ADT σ
EBRT Alone
EBRT Alone σ
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HDR and ADT
HDR σ
EBRT, Seeds, and ADT
EBRT, Seeds, and ADT σ
Hypo EBRT
HIFU
Cryo
Worse <-- Treatment Success --> Better
% PSA Progression Free
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2.5
5
7.5
10
12.5
15
17.5
20
Shorter <-- Years from treatment --> Longer
Highcharts.com

Observations

- For most low-risk patients, most therapies will be successful.
- Treatments at the top of the results comparison graphs for the long periods of years, indicate that patients treated with these methods did not experience an increase in PSA after treatment. These patients are more likely to remain *Prostate Cancer Free*®. Patients are encouraged to look at graphs and determine for themselves.
- Serious side-effect rates must be considered for any treatment.

Risk Group Definitions

Low Risk

Stage: T1 or T2a,b
Gleason Score ≤ 6
PSA ≤ 10 ng/ml

Intermediate Risk

Stage T1 or T1-2
Gleason Score 7
PSA < 10

or

Stage T1-2
Gleason Score 6
PSA 10-20

High Risk

Stage T2c or T3
Gleason Score ≥ 8
PSA > 20 ng/mL

For Questions or More Information

- Prostate Cancer Treatment Research Foundation website: www.pctrf.org
- Contact the Prostate Cancer Treatment Research Foundation: information@pctrf.org
- Additional information for Study Group members: www.pctrf.org/study-group-members/