Prostate Cancer Treatment with Irreversible Electroporation:

Experience in more than 300 patients over 4.5 years

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Publication of this document

- This document is based on the presentation which was given on the World Congress On Electroporation and Pulsed Electric Fields in Biology, Medicine, and Food and Environmental Technologies by Michael K. Stehling MD PhD, on September 8th 2015
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- For the online publication of this document the slides has been edited and comments have been added
- The statistics shown in this document will not be updated

Motivation for Treating PCa with IRE

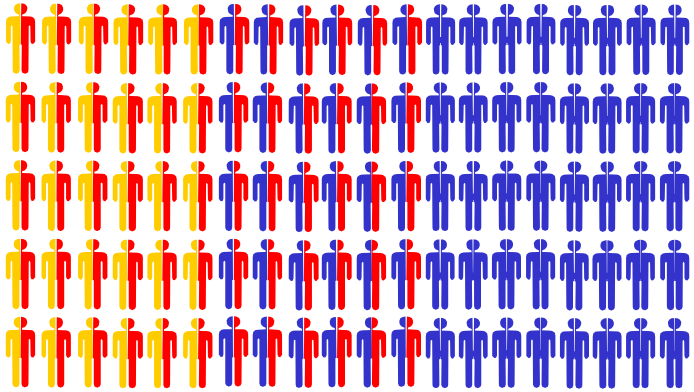
10 year cancer specific mortality rate of low/intermediate-risk PCa: 44,694 patients, 1992 – 2005, SEER database

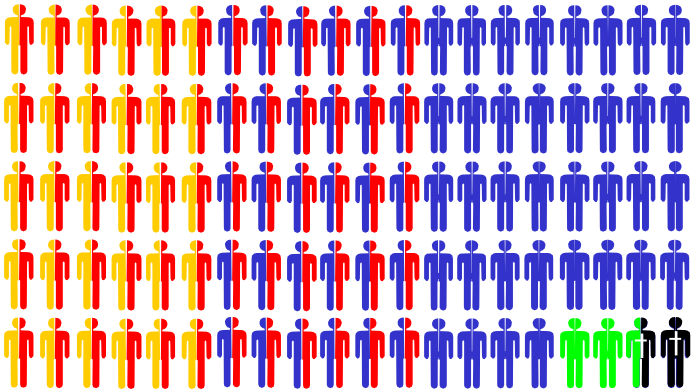
Time of Diagnosis

10 Years Later

Group 1:

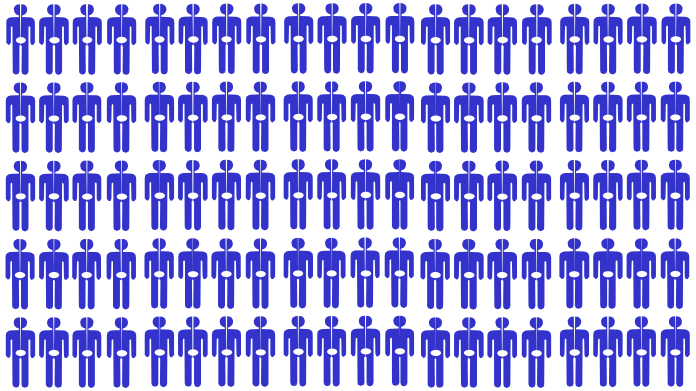
Radical Prostatectomy

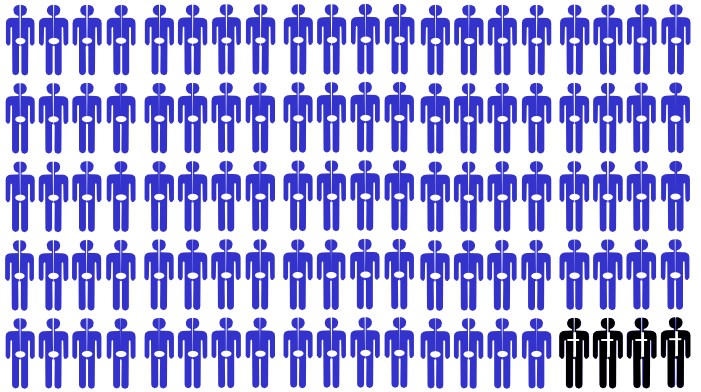




Group 2:

No Treatment
Observation Only





Comments:

This is a visualization of the average numbers for radical prostatectomy.

The doctrine that it is “surgery or die“ is not correct for every grade and stage of PCa. However, for some grades and stages, radical prostatectomy has at least some survival benefit. Every new treatment has to live up to this. But it takes years or decades to prove survival benefit for a new technology as should be obvious from these numbers.

There is an unquestioned side effect profile of prostatectomy, yet there is a constant debate in the scientific literature but also in the media and especially in patient groups. However, the perception of these side effects is very individual.


Incontinent and impotent after Prostatectomy


Impotent after Prostatectomy


Patient with no or only partial incontinence and impotence after Prostatectomy


Patient who chose not to treat at all


Survived Pca thanks to Prostatectomy


Death due to PCa

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Abdollah F, Sun M, Schmitges J, et al. Survival Benefit of Radical Prostatectomy in Patients with Localized Prostate Cancer: Estimations of the Number Needed to Treat According to Tumor and Patient Characteristics. The Journal of Urology, 2012, V188, I1, p73–83

Our Patient Selection for IRE of PCa

Inclusion Criteria

- **Patients who refused standard therapies** (surgery, Rx, AHT)

  Main goal: preservation of erectile function and/or urinary continence

- PCa T1 – T4, any N and M

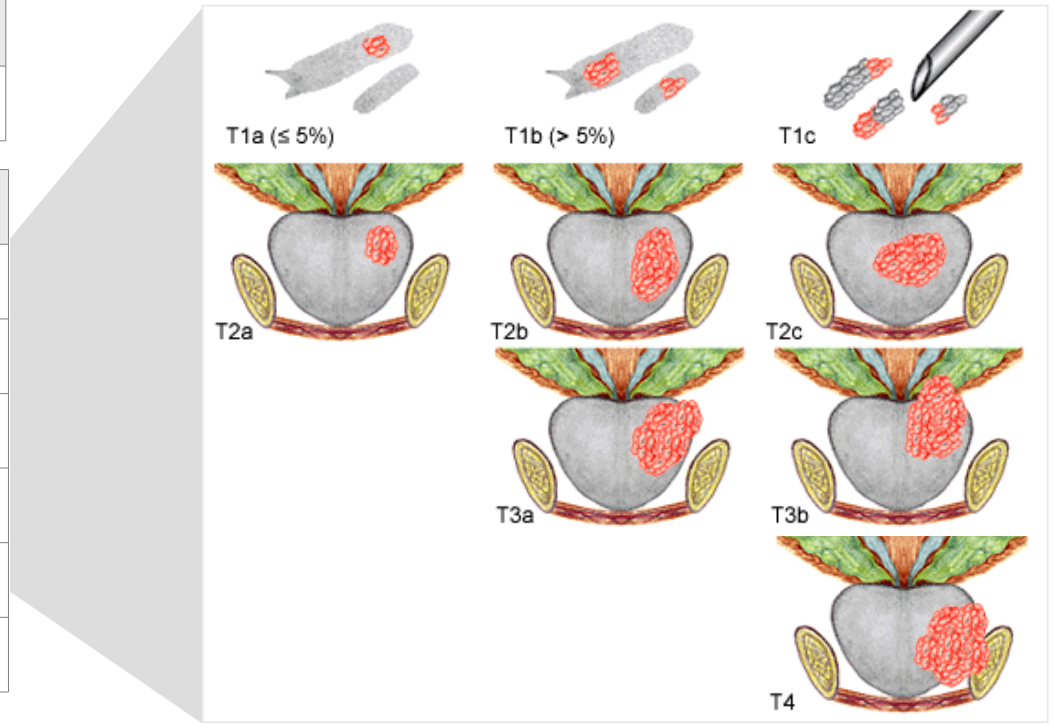
Exclusion Criteria

- Patients unfit for general anaesthesia
- Patients with defibrillators and pacemakers

Our Patient Cohort:
265/302 men with PCa, age 46 - 84

D'Amico Risk Classification	**low**	**intermediate**	**high**	**N/A**
	24	65	164	12
Gleason Score	**6**	**7 (a/b)**	**> 7 (8,9,10)**	**N/A**
	55	117 (89/28)	67 (41/22/4)	26

TNM Stage	**Number of patients**
T1a - T1c	23
T2a - T2c	166
T3a - T3b	44
T4 N0 M0	29
T4 N1 M0 / T4 N0 M1 / T4 N1 M1	25
N/A (BPH treatment)	3



Patient Follow-Up After IRE

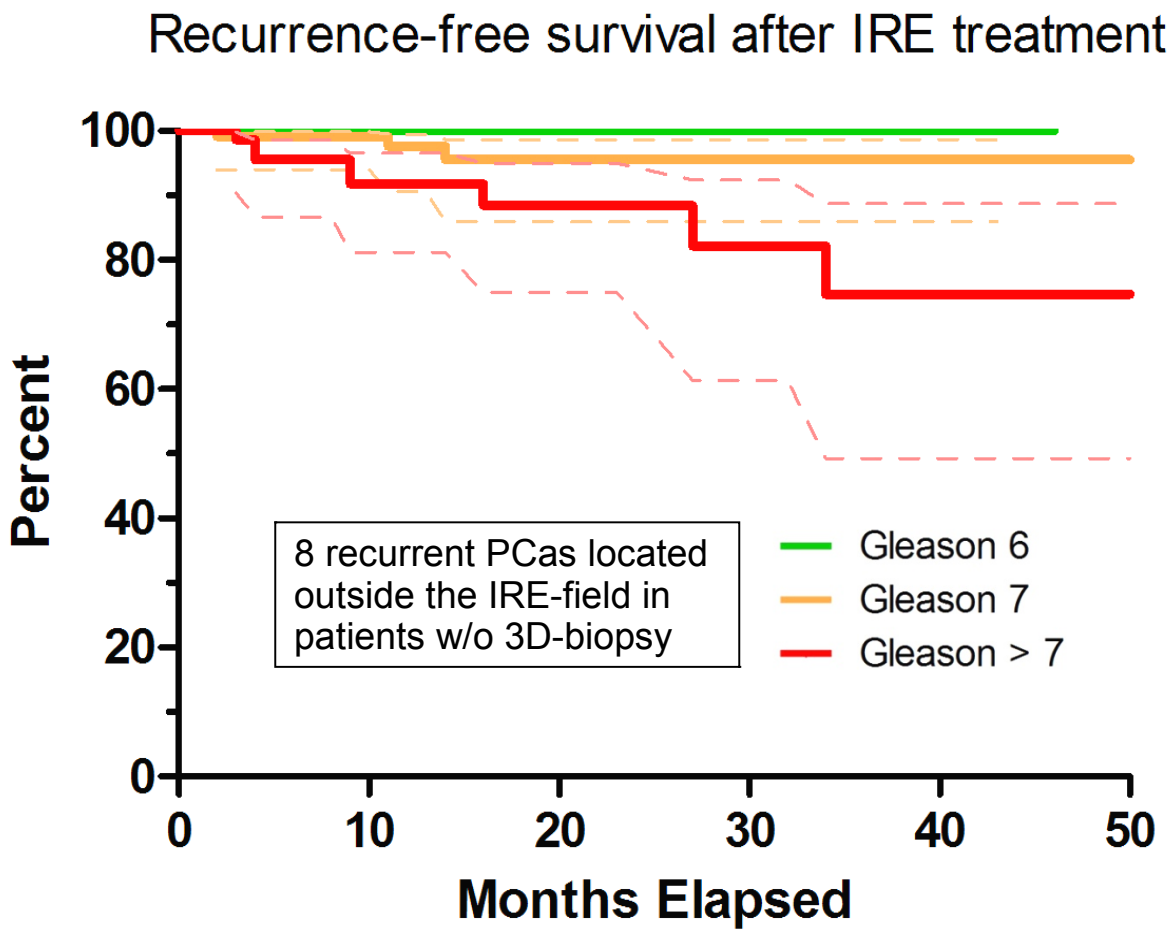
Requested

- MRI at 1 day, 3, 6 and 12 months after IRE, then yearly
- PSA at 3, 6 and 12 months after IRE, then every 3 – 6 months
- Immediate feedback from patients on procedure related complications
- Urinary Incontinence (ICIQ) and Impotence Questionnaire (IIEF-5) (subgroup)

Other

- Cholin or PSMA-PET/CT
- Telephone follow-up for adverse effects, impotence, incontinence
- Re-biopsies only in cases, where PSA and MRI suggested recurrent PCa

Locally recurrent PCa after IRE: 13/265 (max. 50 months follow-up)



D'Amico Risk Classification	low	intermediate	high
IRE as primary PCa treatment	-	-	7
IRE for treatment of recurrent PCa	-	1	5
T-Stage	**T1a - T2b**	**T2c**	**T3a - T4**
IRE as primary treatment	2	1	4
IRE for treatment of recurrent PCa	2	1	3

Comments:

Shown are the Kaplan-Meier curves for recurrence-free survival of the 265 evaluated patients.

As expected, high-risk (Gleason >7) PCa patients have the highest chance of recurrent disease.

Most affected patients refused a workup including a full 3D-mapping biopsy. However, a complete diagnostic workup is essential for good results. This should be respected for every study on IRE, because the study will primarily give insight to patient selection and thorough treatment planning, and only secondary the IRE procedure itself.

All recurrent patients asked for re-treatment with IRE, which never posed to be a problem. No double-recurrence has occurred so far.

Dashed lines show the error margin.

Urinary Continence after IRE

Subjective Assessment of Urinary Continence Patients were asked at the time of Foley catheter removal, during follow-up visits and/or by telephone whether they had „normal urinary bladder function or were losing urine in an uncontrolled way“. Slight „urge incontinence“ within the first 3 months after IRE was accepted. Patients with incontinence before IRE were excluded.	Number of Patients
Incontinence	0/262 (0%)

Erectile Function after IRE

Assessment of Erectile Function by IIEF-5 Questionnaire Before (no ED, ≥ 22P) and after IRE (Δt(**mean**) = 133 days (± 127; 42 - 529))	Number of patients
Severe erectile dysfunction according to IIEF-5 (5-7 P)	0/25 (0%)
Reduction of erectile function (8-21 P, average 6 P, sigma 5 P, P< 0.01)	18/25 (72%)
No change of erectile function	3/25 (12%)
Improvement erectile function (?)	4/25 (16%)

Subjective Assessment of Erectile Dysfunction Patients were asked during follow-up visits or by telephone whether they had 1. a negative change of erectile function related to IRE and 2. were unable to have an erection during sex (with Viagra, Cialis, etc.) and had no spontaneous erection at night, either. Patients with both were classified as having an „IRE related significant erectile dysfunction“.	Number of patients
Transient (up to 9 month) significant erectile dysfunction	27/203 (13.3%)
Persistent (> 9 months) significant erectile dysfunction	8/112 (7.1%)

Comments:

Assessing erectile function is extremely complicated. About 60% of the man in the shown age group have erectile dysfunctions. Many psychology publications show how men notoriously lie about it. It may be more insightful to let their wives fill out the questionnaires, however not every patient is accompanied by their wife when filling out the form.

Even more problematic is the extraordinary high nocebo effect rate: Telling a man about possible impotence as a side effect of a treatment will result in 25-30% of patients to have an erectile dysfunction (Sylvestryi 2003, Cocco 2009).

However, we tried evaluation in two ways. The upper table shows results from the IIEF5 questionnaires. Selected were only patients who filled them out completely and without obvious discrepancies (like full potency under full hormonal blockade) and with at least 22P before treatment. Using the same standard that is used for surgical treatments, 0% got a „severe erectile dysfunction“. This includes 7 patients with whole gland ablations.

Probably more representative is the assessment shown in the lower table. Here we evaluated “negative change in potency“ in personal talks to the patient for a large number of patients.

Rosen RC, Cappelleri JC, Smith MD, et al. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. Int J Impot Res. 1999 Dec;11(6):319-26. © 1999