HDR Brachytherapy for Prostate Cancer: What We Need to Know

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Disclosures

• None
HDR Brachytherapy

- History and Definitions
- Radio biologic Rationale
- Technique and technical notes
- Value to a Urologist and Urology practice
- Efficacy / Comparative Effectiveness
- Toxicity
- Future Directions
History and Definitions
Brachytherapy

• from the Greek word *brachys*, meaning "short-distance"
• also known as internal radiotherapy
• Radiotherapy where a radiation source is placed inside or next to the area requiring treatment
<table>
<thead>
<tr>
<th>Year</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1898</td>
<td>Mme Curie discovers radium</td>
</tr>
<tr>
<td>1901</td>
<td>Curie told to put radium near tumor</td>
</tr>
<tr>
<td>1911</td>
<td>Pasteau and Degrais catheter method at MSK</td>
</tr>
<tr>
<td>1914</td>
<td>H. H. Young modifies Pasteau technique</td>
</tr>
<tr>
<td>1915</td>
<td>Barringer develops interstitial technique</td>
</tr>
<tr>
<td>1952</td>
<td>Iridium – 192 used</td>
</tr>
<tr>
<td>1963-66</td>
<td>High dose rate Ir – 192 introduced</td>
</tr>
<tr>
<td>1970s</td>
<td>Modern I-125 “seeds” used</td>
</tr>
<tr>
<td>1980s</td>
<td>TRUS based LDR/HDR implants</td>
</tr>
<tr>
<td>2000</td>
<td>Image guided dose based treatment planning</td>
</tr>
</tbody>
</table>
Brachytherapy: Early days

Do you recognize this man?
Brachytherapy: Early days

HH Young

• Hopkins Urologist
• Credited with conceiving the radical perineal prostatectomy and also interstitial brachtherapy
Brachytherapy: Early Days

Do you recognize this man?
Brachytherapy: Early Days

• Dr. Willet Whitmore, the father of urologic oncology and seed therapy, is perhaps best remembered for his question: “For a patient with prostate cancer, if treatment for cure is necessary, is it possible? If possible, is it necessary?”
Early Seed Technique

Whitmore, 1960
Early Results

Results:

- 351 cases
- 5.7% alive beyond five years
- “more urinary difficulties...than radical prostatectomy.”

Barringer, 1950
Clinical Therapeutic Radiology
“This therapy has largely gone into the discard because of the few cases controlled, the difficulties in having adequate radon supplies at hand, and the painstaking, persistent work required to treat patients.”

Barringer, 1950
Clinical Therapeutic Radiology
Modern HDR Brachytherapy

High dose rate:

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Dose rate</th>
<th>T1/2</th>
<th>Energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ir-192</td>
<td>1 Gy / min</td>
<td>74d</td>
<td>360 Kev</td>
</tr>
</tbody>
</table>

Low dose rate:

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Dose Rate</th>
<th>T1/2</th>
<th>Energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-125</td>
<td>0.07 Gy/hr</td>
<td>60d</td>
<td>28 Kev</td>
</tr>
<tr>
<td>Pd-103</td>
<td>0.19 Gy/hr</td>
<td>17d</td>
<td>21 Kev</td>
</tr>
</tbody>
</table>
“Modern” HDR Brachytherapy

“Modern” technique (since 1980)

1. Small source
2. Image-based Targeting
3. Perineal Template
4. Treatment Planning Software (greatest evolution)
HDR Brachytherapy
Modern HDR Brachytherapy
Small source, image based targeting via template
Modern HDR Brachytherapy
Complex treatment planning systems control source and deliver treatment
Rationale
HDR Brachytherapy

Radiobiologic rationale:

The main target for ionizing radiation is DNA. Damage leads to mitotic catastrophe which is correlated with PSA production. As cell arrest and then death occurs, PSA drops. PSA levels correlate with ionizing radiation dose. i.e. dose matters

Brenner and Hall: IJROBP, 43:1095, 1999
HDR Brachytherapy

Radiobiologic rationale:

Higher PSA, and higher tumor burden requires more ionizing radiation for the same clinical effect and cellular inactivation.

With higher risk dz, dose matters even more.

Brenner and Hall: IJROBP, 43:1095, 1999
HDR Brachytherapy

Radiobiologic rationale:

• $\alpha/\beta$ value is quantitative measure of an organ/cell’s ability to recover from ionizing radiation

• Response to ionizing radiation varies between body tissue and tumor

• Some tumors respond better to one or two fractions than prolonged fractionation and vice versa

Brenner and Hall: IJROBP, 43:1095, 1999
## Biologic Effective Dose or BED

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosing</th>
<th>1.5 $\alpha/\beta$ (nl tissue)</th>
<th>3 $\alpha/\beta$</th>
<th>10 $\alpha/\beta$ (tumor)</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBRT</td>
<td>81 Gy</td>
<td>174</td>
<td>130</td>
<td>96</td>
<td>Comparing: For the same patient ($2^{nd}$) fractionated dose is less, and the single fraction is more</td>
</tr>
<tr>
<td>Ir 192</td>
<td>2 x 13.5 Gy</td>
<td>270</td>
<td>148</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>EBRT + Ir 192</td>
<td>45 + 10Gy x2</td>
<td>252</td>
<td>160</td>
<td>93</td>
<td>Dose escalation without toxicity</td>
</tr>
</tbody>
</table>
HDR Brachytherapy

For prostate brachytherapy the implication is that HDR treatments, at the appropriately reduced dose, would be expected to be more efficacious than EBRT, but might have less morbidity.
Why I use it and how
Technique
The Process of Quality Assurance in Brachytherapy

1. Patient selection
2. Simulation / Quality Assurance
3. Implant technique
4. Implant planning
5. Treatment evaluation
6. Outcome assessment
nanos gigantum humeris insidentes

- discovering truth by building on previous discoveries
- standing on the shoulders of giants

Bernard of Charters, Newton, Traditional
### Selection

In practice, general guidelines to consider:

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Brachy alone</th>
<th>Combo</th>
<th>+ ADT</th>
<th>Clinical Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Surveillance</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Yes/No/Optional</td>
<td>No/Optional</td>
<td>No</td>
<td>RTOG 0815</td>
</tr>
<tr>
<td>1 risk feature</td>
<td>Yes/No/Optional</td>
<td>No/Optional</td>
<td>No/Yes 4-6 months</td>
<td></td>
</tr>
<tr>
<td>2 risk features</td>
<td>No/Optional</td>
<td>Yes</td>
<td>Yes</td>
<td>RTOG 0924</td>
</tr>
<tr>
<td>or &gt;50% cores</td>
<td>Yes/No/Optional</td>
<td>No/Optional</td>
<td>Yes 6-30 months</td>
<td></td>
</tr>
</tbody>
</table>
## Quality Assurance Documentation

<table>
<thead>
<tr>
<th>Initial/Check</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consult</td>
<td>[Consult 28/80]</td>
</tr>
<tr>
<td>Pubic arch interference (CT)</td>
<td>[Procedure 65]</td>
</tr>
<tr>
<td>TRUS – (Volume study/Simulation):</td>
<td>[Procedure 65]</td>
</tr>
<tr>
<td>Treatment planning</td>
<td>[TP note 31]</td>
</tr>
<tr>
<td>Signed prescription (Mosaiq):</td>
<td>Physician</td>
</tr>
<tr>
<td>Signed plan:</td>
<td>Physician, Physics, Dosimetry</td>
</tr>
<tr>
<td>Seeds/needles ordered (Radioactive Sample Record)</td>
<td></td>
</tr>
<tr>
<td>Physicist verifies and signs vendor documentation and quality assurance</td>
<td></td>
</tr>
<tr>
<td>Physicist compares autoradiograph to needle loading diagram and signs radiograph</td>
<td></td>
</tr>
<tr>
<td>Pre-op Assessment</td>
<td>[pre-op note H&amp;P]</td>
</tr>
<tr>
<td>Implant</td>
<td>[Op note 60]</td>
</tr>
<tr>
<td>Physics note in Progress Notes</td>
<td></td>
</tr>
<tr>
<td>Post-implant Day 0 (CT-based Dosimetry):</td>
<td></td>
</tr>
<tr>
<td>Signed plan:</td>
<td>Physician, Physics, Dosimetry</td>
</tr>
<tr>
<td>QA conference:</td>
<td>[QA note 22]</td>
</tr>
<tr>
<td>Post-implant Day 30 (CT/MRI-based dosimetry)</td>
<td></td>
</tr>
<tr>
<td>Signed plan:</td>
<td>Physician, Physics, Dosimetry</td>
</tr>
<tr>
<td>EMR:</td>
<td>Reviewed &amp; signed plans are scanned into Mosaiq</td>
</tr>
<tr>
<td>Follow-up – EPIC</td>
<td>[Clinic note 53]: 1mo, 4mo, 8mo, 12mo, q6mo to 4 yrs, then annually</td>
</tr>
<tr>
<td>Orders (U/S, CT, Pre-op, Post-op)</td>
<td></td>
</tr>
</tbody>
</table>
Patient Selection

• Inclusion
  – No pelvic LNs or metastasis, life expectancy >5 yrs

• Exclusion (relative)
  – Extensive TURP defect
  – Severe pubic arch interference
  – Unacceptable operative risk
  – Inflammatory bowel disease
  – Ataxia telangiectasia
  – Immunosuppressive drugs, substantial median lobe, very severe obstructive symptoms
Patient Selection vs. LDR

- May implant bigger glands
- May have less acute urinary issues
- TURP defect is not an issue, even protective
- 2 procedures instead of 1
- Better for higher risk and bulkier disease (vs LDR or IMRT)
Issues with HDR

- Still brachytherapy, and at a very high dose
- Patient movement issues, still
- You have to have an excellent physicist who likes to be around/touch/interact with patients (and nurses)
- Pubic arch is still an obstacle to a good implant
- Prostate on CT is hard to define, need tricks
  - Gold markers, U/S fusion, MRI
- Concern for urethral strictures
- Need end to end QA of the entire process
TRUS flexible needle catheter placement, and CT confirmation

Template is secured to perineum until completion
TRUS flexible needle catheter placement, and CT confirmation
U/S guided sagittal needle depth
Post implant Pre treatment planning
CT Scan
Treatment Planning:
Emory SJH Dose and Constraints

Dose Schedule: Mono, 13.5 Gy x 2, 1-2 weeks a part
Boost, 10.5 Gy x 2, 1-2 weeks a part, sequence
15 Gy x 1 on study, RTOG 0815, 0924

**Prostate**
- D90 > 100%
- V100 > 95%
- V200 < 25cc
- V150 < 50cc

**Bladder**
- V75% < 1cc
- D2cc < 80%

**Rectum**
- Urethra+2mm
  - V115% < 1cc
  - D10% < 115%
- V65% < 1cc
  (as low as possible)
- D2cc < 75%
Target Volume = Prostate plus a margin of 2-5 mm gets 13.5 Gy, About a 15 minute treatment
Benefits to a Urology practice

• Effective treatment for all risk groups
• Known, acceptable toxicity profile
• Short treatment times, short recovery
• Most patients are candidates
• Great way for junior colleagues to build on oncologic reputation in a community
Benefits to a Urology Practice

• Minimal OR time needed, < 1 hour per procedure, hospital and free standing centers
• Cost effective; but with a fair \( \triangle \) between the cost (up front and downstream) and reimbursement
• Urologist OR time maybe 30 min or less
• If RVU based, favorable versus LDR/RP
• Remain member of patients entire cancer care
• 2 procedures that work well
And...

Efficacy
Evidence Base Medicine

Climb the Pyramid!!

Hierarchy of Evidence

- Systematic Reviews
- Randomized Controlled Trials
- Cohort Studies
- Case Reports
- Expert Opinion

### Monotherapy: Select series with long term outcome

<table>
<thead>
<tr>
<th># of Series</th>
<th>N</th>
<th>Follow-up</th>
<th>Biochemical Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>1435</td>
<td>60 (53-65) months</td>
<td>Low: 85-97%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Intermediate: 75-93%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>High: 79-93%</td>
</tr>
</tbody>
</table>

Shah, Hoskin, Zamboglou, Yoshioka, Demanes
Outcome: HDR Monotherapy

- Monotherapy – Zamboglou (Germany) Experience
- 718 patients with a median follow up of 53 months
- Risk Grouping: *Used MSKCC criteria
  - 2% Gleason score > 7
  - 1% PSA > 20 ng/ml
  - Mostly low and favorable intermediate risk

Zamboglou, IJROBP, 2012
## Outcome: EBRT with HDR

<table>
<thead>
<tr>
<th>Author/Design</th>
<th># of Patients</th>
<th>Follow up</th>
<th>BC</th>
<th>MFS</th>
<th>Late Toxicity &gt; Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zamboglou/retrospective</td>
<td>718</td>
<td>53 months</td>
<td>94</td>
<td>90</td>
<td>98</td>
</tr>
</tbody>
</table>
Outcome: EBRT + HDR

Combination treatment, EBRT with HDR boost

<table>
<thead>
<tr>
<th># of Series</th>
<th>N</th>
<th>Follow-up</th>
<th>PSA DFS by Risk Group</th>
</tr>
</thead>
</table>
| 12         | 2054| 71 (61-105) months | Low: 92-100%  
Intermediate: 83-100%  
High: 57-97% |

Khor, Cury, Prada, Kotecha, Kaprealian, Savdie, Aluwini, Agoston, Morton, Pellizzon, Ghadjar, Zwahlen
Outcome: EBRT + HDR

- Combination - Galalae IJROBP 2004
- Outcome data from 3 studies
- Prospective phase II, 611 patients
- Risk Grouping: High risk = Any 2 risk factors higher than T2b, iPSA 10, Gleason > 7 disease
- >50% with 2+ high risk features
- 8% low risk, 31% with one intermediate risk feature
- 61% High risk by NCCN, D’Amico

Galalae, IJROBP, 2004
Outcome: EBRT + HDR

5yr PSA control was 77% (10yr 73%)

<table>
<thead>
<tr>
<th># of patients</th>
<th>Follow up</th>
<th>BC</th>
<th>Local control (DRE or Bx)</th>
<th>CSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 611</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By Risk Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>46</td>
<td>96%</td>
<td>0%</td>
<td>100%</td>
</tr>
<tr>
<td>Intermediate</td>
<td>188</td>
<td>88</td>
<td>3.5</td>
<td>99</td>
</tr>
<tr>
<td>High</td>
<td>359</td>
<td>69</td>
<td>10</td>
<td>95</td>
</tr>
</tbody>
</table>

- Predictors of BC on MVI:
  - Gleason score, PSA, Stage, Risk Group
  - But not ADT

Galalae, IJROBP, 2004
HDR: Outcome data

Galalae IJROBP 2004

Authors conclusion

– EBRT+HDR with excellent LT BC, CSS results
– Best reported BC for HR patients to date
– Reproducible
– ADT no benefit

Limitations

– No comparison
– Toxicity lacks data
HDR vs. LDR. Comparable series? Same physicians, same OR. HDR better for T3 dz?

Galalae IJROBP 2004, Sylvester IJROBP 2007
Comparative Effectiveness
Outcome: EBRT vs HDR

- Deutsh, retrospective, MSKCC experience
- Ultra high dose IMRT (86.4Gy) to EBRT with HDR alone/HDR boost
- 650 patients with 50 months follow up

For entire cohort, at median follow up, 80 v 95% with PSA control (p<0.0001)

Deutsh, Zelefsky, Yamada, et al, Brachytherapy, 2010
Outcome: EBRT vs HDR

- 650 pts with long term follow up
- The 5-year actuarial PSA relapse-free survival (PRFS) for HDR plus IMRT vs. ultra-high-dose IMRT:
  - Low risk: 100% vs. 98%
  - Intermed: 98% vs. 84%
  - High risk: 93% vs. 71%

Deutsh, Zelefsky, Yamada, et al, Brachytherapy, 2010
Outcome: EBRT vs. EBRT/HDR

- Hoskin (UK experience)
- RCT, EBRT v EBRT+HDR
- 1997-2005, 218 patients enrolled
- RFS, OS, Toxicity (GU/GI) as endpoints
- 54% high risk, >50% cT3 and/or PSA>20
- Median f/u is 85 m
- At 7 yrs, BFS is 48% in control vs. 66% with HDR

Hoskin, RO, 2012
31% reduction
Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate and high risk prostate cancer treatment by radical therapy. Results from the Prostate Cancer Results Study Group

Peter Grimm¹, Ignace Billiet², David Bostwick³, Adam P. Dicker⁴, Steven Frank⁵, Jos Immerzeel⁶, Mira Keyes⁷, Patrick Kupelian⁸, W. Robert Lee⁹, Stefan Machtens¹⁰, Jyoti Mayadev¹¹, Brian J. Moran¹², Gregory Merrick¹³, Jeremy Millar¹⁴, Mack Roach¹⁵, Richard Stock¹⁶, Katsuma Shintoh¹⁵, Mark Scholz¹⁷, Ed Weber¹⁸

• Few comparative studies exist to date
• Large scale comprehensive review of the published by risk grouping, treatment option and follow up; assessed by PSA outcome

Grimm BJU 2012
Low Risk
Intermediate Risk
High Risk

![Graph showing PSA free progression vs. maximum follow-up years for different treatment methods.](image-url)
Toxicity
HDR: Toxicity

Grills J Urol 2004

Purpose: Compare LDR and HDR

MM: WBH, 1999-2001, 149 pts

- Retrospective
- Monotherapy: HDR (38Gy/4fx) vs Pd103 LDR (120Gy)
- CTCv2
HDR: Toxicity

Grills J Urol 2004

Results

- f/u 35 mos
- Balanced population
- Acute tox: Less Gr 3 with HDR (25v10%), less dysuria, frequency and retention
- Late: HDR stricture 8v3%
  - Gr 2 GU 23v21%, no Gr 4 toxicity; less AUC for HDR
  - Gr 2 GI 0% v 3%
- ED: 16% with HDR, 45% with LDR

Conclusion: HDR wins
Toxicity: HDR Monotherapy

- Monotherapy – Ghilezan WBH Series
- 94 patients prospectively studied for toxicity and outcome on HDR monotherapy protocol
- 17 months follow up
- Acute Toxicity
  - Frequency and urgency common
  - GI issues uncommon
  - No patient required a foley catheter

Ghilezan, IJROBP, 2012
# Toxicity: HDR Monotherapy

## Gastrointestinal

<table>
<thead>
<tr>
<th>Late Toxicity</th>
<th>N = 94</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>1.1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Rectal Bleeding</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Proctitis</td>
<td>2.2</td>
<td>1.1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>5.3</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

## Genitourinary

<table>
<thead>
<tr>
<th>Late Toxicity</th>
<th>N = 94</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysuria</td>
<td>4.3</td>
<td>1.1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Urgency</td>
<td>16.1</td>
<td>1.1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Retention</td>
<td>18</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Incontinence</td>
<td>1.1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Stricture</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Ghilezan, IJROBP, 2012
Toxicity: EBRT + HDR

Combination - Hsu IJROBP 2010

- 112 patients treated on a Phase II RTOG study treated at 14 institutions with a median follow up of 30 months

- Acute Grade 3 events occurred 3 patients
- Late Grade 3 events occurred 4 patients
- Risk of late Grade 3-5 toxicity at 18 months was 2.5%

- Common side effects included urinary frequency, retention, ED, cystitis, proctitis
- Erectile dysfunction: 26 Grade 2, 5 Grade 3 reported
Patient Reported Outcomes

Sanda, NEJM, 2008
(+HDR, Morton, 2013)

- PR QOL via EPIC
- % change in report of distress or dysfunction on EPIC at 2 years
Conclusion of Efficacy and Toxicity

- HDR brachytherapy has level I, II, and abundant retrospective data substantiating efficacy.
- HDR Brachytherapy, as a part of therapy, is associated with excellent results for all risk groups.
- HDR Brachytherapy is associated with early urinary bother, which is mostly acute and self-limiting, and better erectile function long term compared to other modalities like IMRT.
- HDR Brachytherapy outcome results (PSA control) are sustained.
Cost Effectiveness
Cost Effectiveness

Purpose

• Economic evaluation examining health outcomes and costs of (competing) intervention strategies

• Focusing on
  – Outcomes
  – Comparable costs and benefit
  – Quality adjusted life expectancy
Costs

• Shah, Brachytherapy, 2012
• 1328 patients who received IMRT, LDR, or HDR, compared for cost effectiveness
• Cost, and Incremental Cost Effectiveness Ratio (ICER) Reported
• ICER = ratio of difference of cost and difference of efficacy
Cost Effectiveness

<table>
<thead>
<tr>
<th>Modality</th>
<th>BC</th>
<th>CSS</th>
<th>Reimbursement</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDR</td>
<td>NS</td>
<td>NS</td>
<td>10K</td>
<td>2.3K</td>
</tr>
<tr>
<td>HDR</td>
<td>NS</td>
<td>NS</td>
<td>17.5K (4fx)</td>
<td>5.5K</td>
</tr>
<tr>
<td>IMRT</td>
<td>NS</td>
<td>NS</td>
<td>29K</td>
<td>23.5K</td>
</tr>
</tbody>
</table>

For reimbursement, LDR < HDR << IMRT, p<0.05
For costs, LDR < HDR << IMRT, p<0.05

ICER by modality for 1% improvement in biochemical control

<table>
<thead>
<tr>
<th></th>
<th>IMRT</th>
<th>LDR</th>
<th>HDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reimbursement</td>
<td>-</td>
<td>4K</td>
<td>3K</td>
</tr>
<tr>
<td>Costs</td>
<td>-</td>
<td>4K</td>
<td>4K</td>
</tr>
</tbody>
</table>

For ICER, or cost effectiveness, LDR and HDR is superior to IMRT, p<0.05

Shah, Brachtherapy, 2012
Quality-adjusted life expectancy (QALE)

- QALE: Measure of disease burden in terms of quantity (easy to measure) and quality (lots of factors) of life lived
- A lot of assumptions in QALE models, which may reflect limitations of outcome data reported in the literature
- Hayes, Ann of Int Med, 2013
Quality-adjusted life expectancy (QALE)

- For 65 yo with LR dz*, with many assumptions*
- Watchful waiting is safe and most cost effective
- BT is least expensive therapy, less than AS
- WW/AS yields best quality adjusted life exp

<table>
<thead>
<tr>
<th>Modality</th>
<th>Costs</th>
<th>Incremental Costs</th>
<th>QALE</th>
<th>Incremental QALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>WW</td>
<td>24K</td>
<td>-</td>
<td>9.0</td>
<td>-</td>
</tr>
<tr>
<td>BT (HDR?)</td>
<td>35K</td>
<td>11K</td>
<td>8.1</td>
<td>-0.9</td>
</tr>
<tr>
<td>RP</td>
<td>38K</td>
<td>14K</td>
<td>8.0</td>
<td>-1.1</td>
</tr>
<tr>
<td>AS</td>
<td>40K</td>
<td>15K</td>
<td>8.9</td>
<td>-0.1</td>
</tr>
<tr>
<td>IMRT</td>
<td>49K</td>
<td>24K</td>
<td>8.1</td>
<td>-0.9</td>
</tr>
</tbody>
</table>
Conclusion: Cost Effectiveness

- HDR outcome and toxicity is comparable to LDR and IMRT
- Like LDR, HDR has similar and perhaps superior cost effectiveness to all therapies, and better QALE than RP or IMRT
Future Directions

- MR based planning
- Grants in image fusion / recognition / auto planning
- Salvage therapy (data)
- Focal therapy (need studies)
- Patient reported Quality of Life
- Vehicle for tissue research
Conclusions: HDR Brachytherapy

• Long history in Urology
• Radio biologic Rationale
• Value to a Urologist
• High efficacy, low toxicity, compares well, cost effective with favorable QOL
• Promising future directions
Salvage HDR
Salvage HDR

UCSF (Chen, Shinohara, Hsu, IJROBP, 2013)

- 52 pts
- Salvage HDR p RT failures
- Median f/u 5yrs
- OS: 92% DMFS: 99%
- LC: 51%
- Late Gr 3: 2% GU
Salvage LDR

NE Florida (Vargas, Terk, Brachytherapy, 2013)

- 69 pts
- Salvage LDR after failure
- Median f/u 5yrs
- LC
  - LR: 86% and IR: 75% and HR: 66%
  - Non CR: 74% and CR: 22%
- GR 3 Toxicity: 9%, all GU
- (Lots of Gr 1,2)
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