

Salvage brachytherapy: do we have consensus?

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Salvage brachytherapy: do we have consensus?

- Patient selection
- LDR or HDR
- Volume
- Dose

Selection for Salvage following previous radical radiotherapy

A Delphi consensus study on salvage brachytherapy for prostate cancer relapse after radiotherapy, a Uro-GEC study

Kaljouw et al [Radiotherapy and Oncology 118 \(2016\) 122-130](#)

N=18

Agreement = >80%.....in 52% options

- No minimum age
- Gleason <8
- NO current ADT
- Stage up to T3b
- 12-24 biopsies
- Evaluate metastases

Salvage prostate brachytherapy in radiorecurrent prostate cancer: An international Delphi consensus study

Corkum et al [Radiotherapy and Oncology 184 \(2023\) 109672](#)

N=30

Agreement >75%in 56% options

- 2-4 years from primary treatment
- Any type of previous RT
- MRI and PSMA PET required
- Targeted and systematic biopsies
- Any Gleason score at relapse

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- NO current ADT
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- 12-24 biopsies
- Evaluate metastases

Divided opinion (65-80%)

- Age<80y; Life expectancy >5y
- PSA DT >6mo
- Prostate volume
- Imaging for biopsies (MR or US)
- Imaging for mets: MR or PET

Failed consensus

- PSA at relapse
- Qmax and RV
- Number of Bx <12 - >24

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Agreement >75%in 56% options

- 2-4 years from primary treatment
- Any type of previous RT
- MRI and PSMA PET required
- Targeted and systematic biopsies
- Any Gleason score at relapse

Failed consensus

- Performance status
- Any T stage
- Oligometastases
- PSA<20
- Urodynamics NOT needed
- IPSS <15-20

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- All participants found HDR suitable.
- A majority (77%) would use LDR (as an alternative treatment if HDR not available)
- 29% would also advocate PDR

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Agreement >75%in 56% options

‘The preferred treatment technique is HDR’

- 70% agreement
- 27% offering both HDR and LDR

Salvage Reirradiation Options for Locally Recurrent Prostate Cancer: A Systematic Review

Zhong et al

Salvage therapy details for BT studies.

First author (country)	Year	Single-centre (1) or Multi-centre (2)	Patients (n)	BT Technique	Radiation Source	Focal or Whole-gland	Dose (total dose (Gy)/ dose per fraction/ number of fractions)	Duration of treatment	Adjuvant ADT	Follow-up (mo) (range)	BC (%)	Oncologic outcomes
B Lee (USA)	2007	1	21	HDR	Ir-192	Whole	36/6/6	7 days	No	18.7	90.8	2-yr bRFS 89%
Lyczek (Poland)	2009	1	115	HDR	Ir-192	Whole	30 / 10 / 3	9 weeks	NR	NR	46 (PSA<6) vs 18 (PSA>6)	OS 86% (PSA<6) vs 48% (PSA>6)
Chen (USA)	2013	1	52	HDR	Ir-192	Whole	36 / 6 / 6	10 days	NR	59.6 (5.9-154.7)	55.7	5-yr bRFS 51%, 5-yr OS 92%
Kukleka (Poland)	2014	1	25	HDR with interstitial hyperthermia	Ir-192	Whole	37/9/4	63 days	Yes (12%)	13 (4-48)	NR	2-yr bRFS 74%
*Yamada (USA)	2014	1	42	HDR	Ir-192	Whole	32 / 8 / 4	30 hours	Yes (43%)	36 (2-66)	68.5	5-yr OS 90.3%
Jiang (Germany)	2016	1	29	HDR	Ir-192	Whole	30 / 10 / 3	3 weeks	Yes (34.5%)	73 (61-140)	45	5-yr bRFS 45%, 5-yr OS 95.5%
Lacy (USA)	2016	1	21	HDR	Ir-192	Whole	108-144 Gy	-	Yes (14.3%)	61 (10-149)	47.6	NR
Wojcieszek (Poland)	2016	1	83	HDR	Ir-192	Whole	30 / 10 / 3	28-30 days	Yes (53%)	41 (11-76)	67	5-yr CSS 87%
Lopez (Spain)	2019	2	75	HDR	Ir-192	Whole	32 / 7-10 / 2-4	-	Yes (45%)	52	67.5	5-yr bRFS 65%
			44	LDR	NR	Whole	145 Gy	-	Yes (532%)	52	68	5-yr bRFS 79%
Chitmanee (UK)	2020	1	50	HDR	Ir-192	Focal	1 x 19 Gy	-	Yes (8%)	21 (1-53)	46	2-yr bRFS 63%, 3-yr bRFS 46%
Slevin (UK)	2020	1	43	HDR	Ir-192	Focal	1 x 19 Gy	-	Yes (74%)	26 (1-60)	79	3-yr bRFS 41.8%
van Son (Netherlands)	2020	1	50	HDR (MRI Guided ultra-focal)	Ir-192	Ultra-focal	1 x 19 Gy	-	Yes (12%)	31 (13-58)	48	2.5 yr bRFS 51%, mFS 75%, OS 98%
Kolmeier (USA)	2017	1	37	LDR	125-I (8%) or 103-Pd (92%)	Whole	125-144 Gy	-	Yes (46%)	31 (2-97)	65	3-yr bRFS 60.2%. 3-yr mFS 78.7%
			61	HDR	Ir-192	Whole	32 / 8 / 4 (n=58), 28 / 7 / 4 (n=1) and 22 / 11 / 2 (n=1)	30 hours	Yes (44%)			
Baumann (USA)	2017	1	33	HDR/LDR	103-Pd (LDR) and Ir-192 (HDR)	Whole	LDR (90-100 Gy) or HDR (30/6/5)	NR	Yes (100%)	61 (7-150)	67	7-yr RFS 67%
Henriquez (Spain)	2014	1	56	HDR/LDR	Ir-192/ 125-I	Whole	HDR: 50.5 / 5.25 / 1-4, LDR: 145 Gy	NR	Yes (26.8%)	48 (25-109)	NR	5-yr bRFS 77%, 5-yr OS 70%
Grado (USA)	1999	1	49	LDR	125-I (76%) or 103-Pd (24%)	Whole	80-180 Gy	-	Yes (16%)	41.7 (21.8-185.2)	34	3-yr bRFS 48%, 5-yr bRFS 34%. LC 98%
Koutrouvelis (USA)	2003	1	31	LDR	125-I (77%) or 103-Pd (23%)	Whole	100-144 Gy	-	No	30 (12-84)	87	3-yr bRFS 83.9%, 5-yr bRFS 41.9%
Nguyen (USA)	2007	1	25	LDR	125-I	Whole	137 Gy	-	No	47 (14-75)	72	4-yr bRFS 70%
HK Lee (USA)	2008	1	21	LDR	103-Pd	Whole	90 Gy	-	Yes (57%)	36	NA	5-yr bRFS 38%, 5-yr OS 81%
Aaronson (USA)	2009	1	24	LDR	125-I or 103-Pd	Whole	146 Gy	-	Yes (29%)	30 (13-65)	87.5	3-yr bRFS 89.5% 3-year CSS 96%
Burri (USA)	2010	1	37	LDR	103-Pd (97%) or 125-I (4%)	Whole	110-135 Gy	-	Yes (84%)	86 (2-156)	NA	5-yr bRFS 65%, 5-yr CSS 94%, 5-yr OS 96%
Moman (Netherlands)	2010	1	31	LDR	125-I	Whole	145 Gy	-	NA	108	19	1-yr bRFS 51%, 5-yr bRFS 20%, 5-yr CSS 74%, 5-yr OS 72%
Peters (Netherlands)	2014	1	20	LDR	125-I	Focal	144 Gy	-	NR	36 (10-45)	71	3-yr bRFS 71%
Vargas (USA)	2014	1	69	LDR	125-I	Whole	100 Gy	-	Yes (90%)	60 (7-164)	68.6	5-yr OS 64%, 5-yr mFS 90%
Peters (Netherlands)	2016	2	62	LDR (Whole Gland)	125-I	Whole	145 Gy	-	Yes (34%)	78 (5-139)	NR	Estimated 10-yr PCaSS 43%, 10-yr OS 34%
Crook (Canada)	2019	2	92	LDR	125-I (92%) or 103-Pd (8%)	Whole	120-140 Gy	-	NR	54	NR	NR
Smith (USA)	2020	2	108	LDR	125-I (1%) or 103-Pd (99%)	Whole	100 Gy	-	Yes (93.5%)	75 (1-228)	NR	5-yr bRFS 63%, 10-yr bRFS 52%
Schonb (Germany)	2020	1	82	PDR	Ir-192	Whole	60 / 30 / 2	4 weeks	Yes (43.9)	49 (12-129)	65.6	5-yr bRFS 65.6%, LC 86.6%

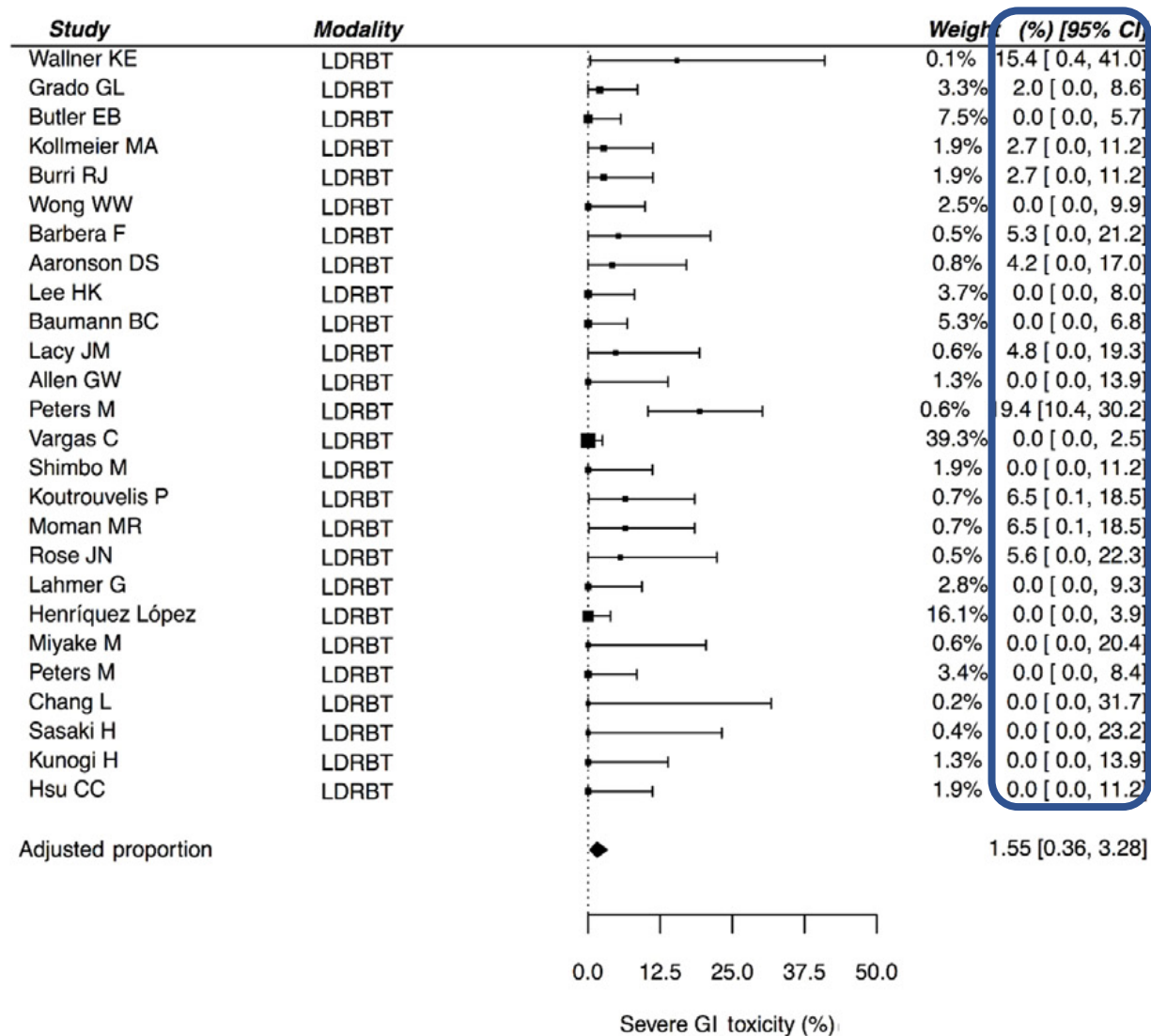
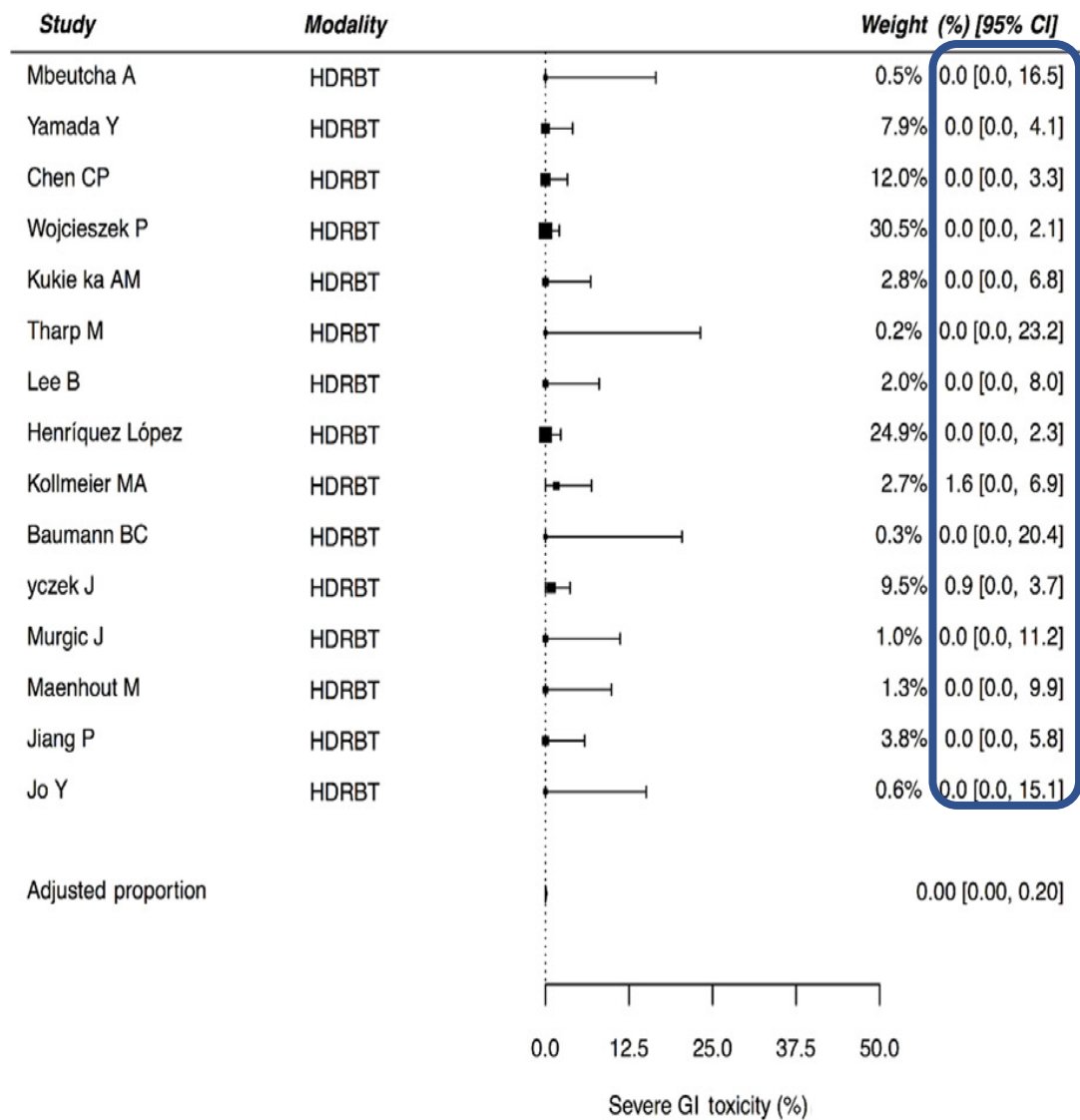
HDR or LDR?

A Systematic Review and Meta-analysis of Local Salvage Therapies After Radiotherapy for Prostate Cancer (MASTER)

EUROPEAN UROLOGY 80 (2021) 280–292

Valle et al

NO severe GI toxicity

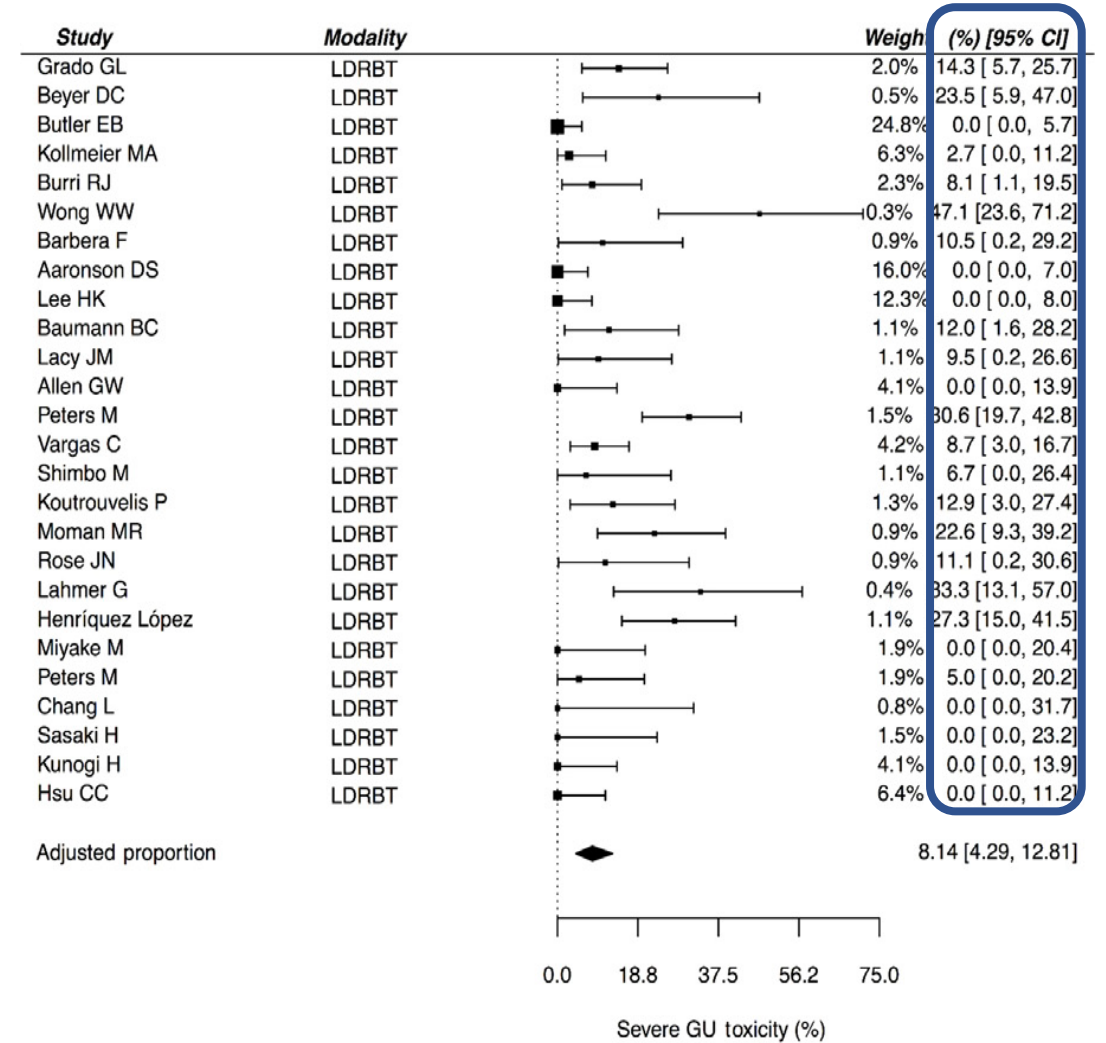
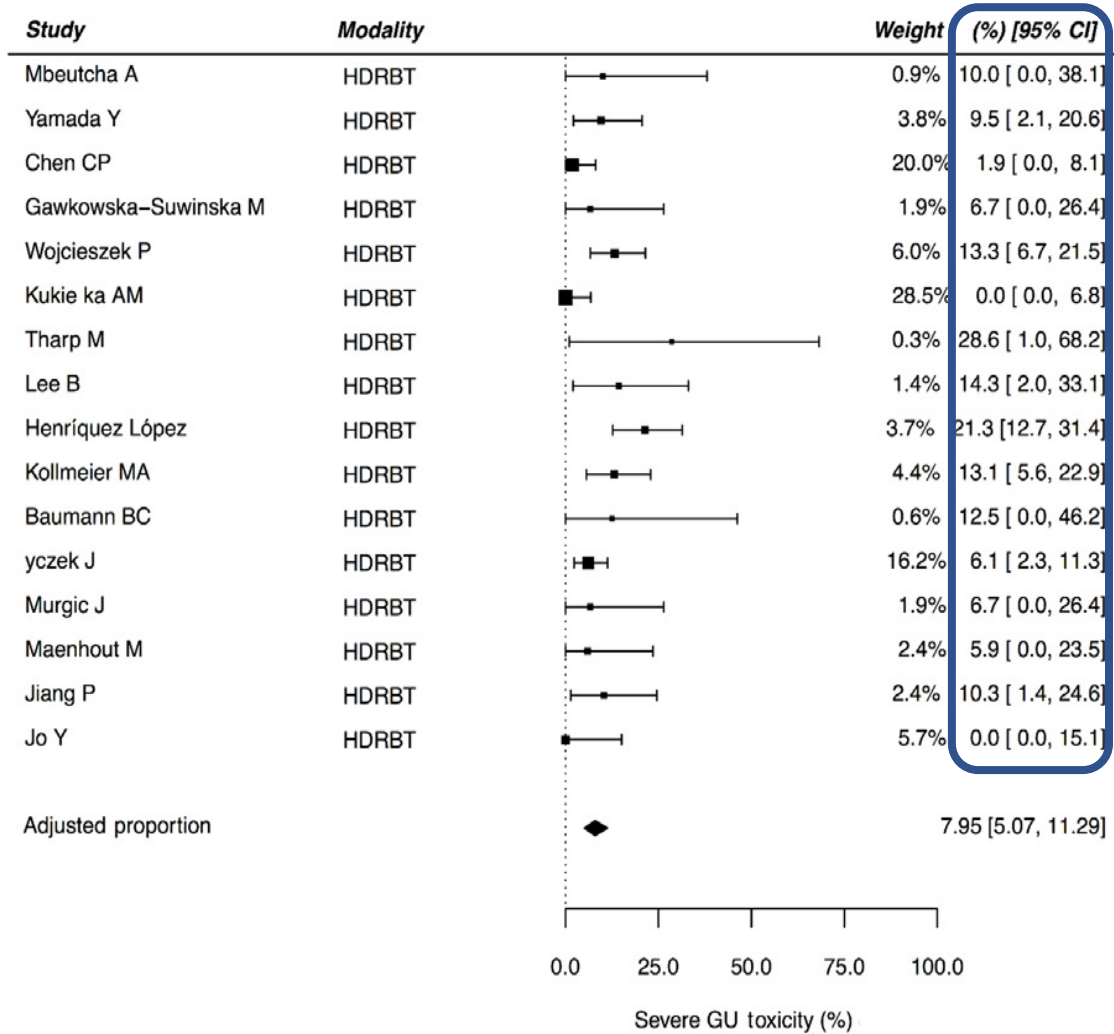


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8% severe GU toxicity



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Covariate-adjusted meta-regression comparing efficacy and toxicity between salvage modalities and radical prostatectomy

	2-yr RFS	5-yr RFS	Severe GU toxicity	Severe GI toxicity
Radical prostatectomy				
Adjusted percent ^a (95% CI)	72% (66–78%)	53% (46–59%)	21% (16–26%)	1.5% (0.4–3.2%)
Odds ratio (95% CI)	1.0	1.0	NA	NA
<i>p</i> value	Reference	Reference	Reference	Reference
R ² (%)	0.0	0.0	0.0	0.0
Cryotherapy				
Adjusted percent ^a (95% CI)	66% (59–72%)	57% (49–65%)	15% (8–23%)	0.9% (0.3–1.8%)
Odds ratio (95% CI)	0.74 (0.49–1.12)	1.20 (0.80–1.79)	NA	NA
<i>p</i> value	0.2	0.4	0.2	0.5
R ² (%)	25	0.0	8.2	27
HIFU				
Adjusted percent ^a (95% CI)	52% (45–59%)	46% (37–55%)	23% (17–30%)	0.8% (0.1–2.1%)
Odds ratio (95% CI)	0.42 (0.28–0.64)	0.76 (0.48–1.21)	NA	NA
<i>p</i> value	<0.001	0.2	0.5	0.4
R ² (%)	0.0	41	15	22
SBRT				
Adjusted percent ^a (95% CI)	58% (46–69%)	56% (37–73%)	5.6% (1.4–12%)	0.0% (0.0–1.2%)
Odds ratio (95% CI)	0.52 (0.30–0.93)	1.13 (0.50–2.58)	NA	NA
<i>p</i> value	0.03	0.8	<0.001	0.07
R ² (%)	55	4.2	0.00	0.0
HDR				
Adjusted percent ^a (95% CI)	77% (69–83%)	58% (52–64%)	9.6% (6.0–13.9%)	0.0% (0.0–0.3%)
Odds ratio (95% CI)	1.26 (0.77–2.09)	1.25 (0.88–1.78)	NA	NA
<i>p</i> value	0.4	0.2	0.002	0.003
R ² (%)	0.0	91	0.0	0.0
LDR				
Adjusted percent ^a (95% CI)	79% (72–85%)	53% (43–63%)	9.1% (5.2–14%)	2.1% (0.6–4.0%)
Odds ratio (95% CI)	1.49 (0.89–2.50)	1.02 (0.63–1.67)	–	–
<i>p</i> value	0.13	0.9	0.001	0.6
R ² (%)	4.3	5.2	12	20%

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N=18

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- Whole gland: 41%
- Hemigland: 12%
- Focal: 47%

- Participants >20 cases/yr: 70%
- Participants <20 cases/yr: 63%

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Agreement >75%in 56% options

‘Salvage can be offered as either whole gland or focal with patient factors deciding choice’

- 73% agreement
- 20% strongly prefer focal

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Schonb (Germany)	2020	1	82	PDR	Ir-192	Whole	60 / 30 / 2	4 weeks	Yes (43.9)	49 (12-129)	65.6	5-yr bRFS 65.6%, LC 86.6%

Whole gland or focal?

A Systematic Review and Meta-analysis of Local Salvage Therapies After Radiotherapy for Prostate Cancer (MASTER) Valle et al

EUROPEAN UROLOGY 80 (2021) 280–292

Summary of patient and treatment characteristics for local salvage modalities

	Age (yr)	Whole-gland salvage (%)	Biopsy-proven recurrence (%)	Presalvage PSA (ng/mL)	Perisalvage ADT use (%)	Interval from initial treatment to recurrence or salvage (mo)	Median follow-up (mo)	Number of studies (n)	Number of patients (n)
RP	65	100	99	6.0	16	50	47	52	2686
Cryotherapy	66	93	99	5.8	35	63	32	32	5153
HIFU	69	86	100	5.0	18	63	33	20	1783
SBRT	72	61	81	4.0	37	89	26	8	261
HDR	71	85	94	4.5	43	61	40	16	586
LDR	69	92	95	5.5	37	67	52	32	853

ADT = androgen deprivation therapy; HDR = high-dose-rate brachytherapy; HIFU = high-intensity focused ultrasound; LDR = low-dose-rate brachytherapy; PSA = prostate-specific antigen; RP = radical prostatectomy; SBRT = stereotactic body radiotherapy.

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N=18

Agreement = >80%.....in 52% options

- Same dose as primary treatment: 63%
- Higher dose: 37%
- Consensus 90-109Gy EQD₂_{1.5}

Dose schedules for a 90–109 Gy EQD₂ dose level calculated for an α/β ratio of 1.5 Gy.

Dose schedule (Gy)	EQD ₂ (Gy)
3 × 9.5	90
2 × 12	93
4 × 8.5	97
3 × 10	99
2 × 13	108
3 × 10.5	108
4 × 9	108

- Dose constraints to OARs: no consensus

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N=30

Agreement >75%in 56% options

‘Modification of target dose is not necessary (depending on time from previous RT and technique)’

- 77% agreement

‘Modification of OAR dose is not necessary (depending on time from previous RT and technique)’

- 93% agreement

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Chitmanee (UK)	2020	1	50	HDR	Ir-192	Focal	1 x 19 Gy	-	Yes (8%)	21 (1-53)	46	2-yr bRFS 63%, 3-yr bRFS 46%
Slevin (UK)	2020	1	43	HDR	Ir-192	Focal	1 x 19 Gy	-	Yes (74%)	26 (1-60)	79	3-yr bRFS 41.8%
van Son (Netherlands)	2020	1	50	HDR (MRI Guided ultra-focal)	Ir-192	Ultra-focal	1 x 19 Gy	-	Yes (12%)	31 (13-58)	48	2.5 yr bRFS 51%, mFS 75%, OS 98%
Kolmeier (USA)	2017	1	37	LDR	125-I (8%) or 103-Pd (92%)	Whole	125-144 Gy	-	Yes (46%)	31 (2-97)	65	3-yr bRFS 60.2%. 3-yr mFS 78.7%
			61	HDR	Ir-192	Whole	32 / 8 / 4 (n=58), 28 / 7 / 4 (n=1) and 22 / 11 / 2 (n=1)	30 hours	Yes (44%)			
Baumann (USA)	2017	1	33	HDR/LDR	103-Pd (LDR) and Ir-192 (HDR)	Whole	LDR (90-100 Gy) or HDR (30/6/5)	NR	Yes (100%)	61 (7-150)	67	7-yr RFS 67%
Henriquez (Spain)	2014	1	56	HDR/LDR	Ir-192/ 125-I	Whole	HDR: 50.5 / 5.25 / 1-4, LDR: 145 Gy	NR	Yes (26.8%)	48 (25-109)	NR	5-yr bRFS 77%, 5-yr OS 70%
Grado (USA)	1999	1	49	LDR	125-I (76%) or 103-Pd (24%)	Whole	80-180 Gy	-	Yes (16%)	41.7 (21.8-185.2)	34	3-yr bRFS 48%, 5-yr bRFS 34%. LC 98%
Koutrouvelis (USA)	2003	1	31	LDR	125-I (77%) or 103-Pd (23%)	Whole	100-144 Gy	-	No	30 (12-84)	87	3-yr bRFS 83.9%, 5-yr bRFS 41.9%
Nguyen (USA)	2007	1	25	LDR	125-I	Whole	137 Gy	-	No	47 (14-75)	72	4-yr bRFS 70%
HK Lee (USA)	2008	1	21	LDR	103-Pd	Whole	90 Gy	-	Yes (57%)	36	NA	5-yr bRFS 38%, 5-yr OS 81%
Aaronson (USA)	2009	1	24	LDR	125-I or 103-Pd	Whole	146 Gy	-	Yes (29%)	30 (13-65)	87.5	3-yr bRFS 89.5% 3-year CSS 96%
Burri (USA)	2010	1	37	LDR	103-Pd (97%) or 125-I (4%)	Whole	110-135 Gy	-	Yes (84%)	86 (2-156)	NA	5-yr bRFS 65%, 5-yr CSS 94%, 5-yr OS 96%
Moman (Netherlands)	2010	1	31	LDR	125-I	Whole	145 Gy	-	NA	108	19	1-yr bRFS 51%, 5-yr bRFS 20%, 5-yr CSS 74%, 5-yr OS 72%
Peters (Netherlands)	2014	1	20	LDR	125-I	Focal	144 Gy	-	NR	36 (10-45)	71	3-yr bRFS 71%
Vargas (USA)	2014	1	69	LDR	125-I	Whole	100 Gy	-	Yes (90%)	60 (7-164)	68.6	5-yr OS 64%, 5-yr mFS 90%
Peters (Netherlands)	2016	2	62	LDR (Whole Gland)	125-I	Whole	145 Gy	-	Yes (34%)	78 (5-139)	NR	Estimated 10-yr PCaSS 43%, 10-yr OS 34%
Crook (Canada)	2019	2	92	LDR	125-I (92%) or 103-Pd (8%)	Whole	120-140 Gy	-	NR	54	NR	NR
Smith (USA)	2020	2	108	LDR	125-I (1%) or 103-Pd (99%)	Whole	100 Gy	-	Yes (93.5%)	75 (1-228)	NR	5-yr bRFS 63%, 10-yr bRFS 52%
Schonb (Germany)	2020	1	82	PDR	Ir-192	Whole	60 / 30 / 2	4 weeks	Yes (43.9)	49 (12-129)	65.6	5-yr bRFS 65.6%, LC 86.6%

DOSE
consensus?

Salvage Reirradiation Options for Locally Recurrent Prostate Cancer: A Systematic Review

Zhong et al

HDR

LDR

Dose(Gy)

Dose/#

Number #

• I125

80-180Gy

36

6

3 days

100-144Gy

30

10

3 days

100Gy

32

8

4 days

144-146Gy

33

7-10

2-4 days

• Pd103

26-27

13-13.5

2 - 8 days

90Gy

19

1

1 day

110Gy

Salvage brachytherapy: do we have consensus?

- Patient selection
- LDR or HDR
- Volume
- Dose

Brachytherapy for salvage?

GEC ESTRO HDR guidelines 2013

HDR in recurrence

There is limited experience of HDR brachytherapy for locally recurrent prostate cancer after previous irradiation and this is not recommended outside a formal prospective study. OAR constraints are critical in this setting. Published schedules (planning aim) include the following:

36 Gy in 6 fractions [44].

21 Gy in 3 fractions [45].

30 Gy in 2 fractions to peripheral zone after 30–40 Gy external beam [46].

ABS guidelines 2013

There is a promising data describing the use of HDR monotherapy as salvage for localized recurrence after prior external beam radiation or permanent seed brachytherapy. The ABS recommends that the use of HDR as salvage therapy be limited to Institutional Review Board-approved protocols or specialty centers with appropriate expertise.

GEC ESTRO HDR guidelines 2023

There remains limited high quality evidence to support salvage therapy with no consistent patient selection criteria, volume or dose recommendations. Salvage brachytherapy should therefore be regarded as investigational to be undertaken within formal research protocols.

Recommendations:

- Salvage brachytherapy is only recommended within the context of a clinical trial.

Grade C, Level 4

Do we have consensus?



LEVELS OF CONSENSUS



Maybe the nearest we will get for now