Article:
Henry, A orcid.org/0000-0002-5379-6618, Pieters, BR, André Siebert, F et al. (2 more authors) (2022) GEC-ESTRO ACROP prostate brachytherapy guidelines. Radiotherapy and Oncology, 167. pp. 244-251. ISSN 0167-8140

https://doi.org/10.1016/j.radonc.2021.12.047

GEC-ESTRO ACROP Prostate Brachytherapy Guidelines

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Highlights

- The purpose of the paper is to update previously published GEC ESTRO guidelines for prostate brachytherapy
- Consensus guidelines are made for Low Dose Rate (LDR) and High Dose Rate (HDR) brachytherapy treatments

Keywords
Brachytherapy
Prostate cancer
Consensus guidelines
Low Dose Rate
High Dose Rate

Abstract

This is an evidence-based guideline for prostate brachytherapy. Throughout levels of evidence quoted are those from the Oxford Centre for Evidence based Medicine (https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009)

Prostate interstitial brachytherapy using either permanent or temporary implantation is an established and evolving treatment technique for non-metastatic prostate cancer.

Permanent brachytherapy uses Low Dose Rate (LDR) sources, most commonly I-125, emitting photon radiation over months. Temporary brachytherapy involves first placing catheters within the prostate and, on confirmation of accurate positioning, temporarily introducing the radioactive source, generally High Dose Rate (HDR) radioactive sources of Ir-192 or less commonly Co-60. Pulsed dose rate (PDR) brachytherapy has also been used for prostate cancer [1] but few centres have adopted this approach. Previous GEC ESTRO recommendations have considered LDR and

HDR separately [2][3][4] but as there is considerable overlap, this paper provides updated guidance for both treatment techniques.

Prostate brachytherapy allows safe radiation dose escalation beyond that achieved using external beam radiotherapy alone as it has greater conformity around the prostate, sparing surrounding rectum, bladder, and penile bulb. In addition there are fewer issues with changes in prostate position during treatment delivery. Systematic review and randomised trials using both techniques as boost treatments demonstrate improved PSA control when compared to external beam radiotherapy alone [5][6][7].

Indications for Prostate Brachytherapy

Prostate brachytherapy is a highly effective treatment for localised prostate cancer in patients who have no evidence of metastases. It is indicated in two settings:

- *Alone* as sole modality for low and selected intermediate risk prostate cancer.
- *Combined* to dose escalate with external beam radiotherapy for intermediate and high risk prostate cancer

Detailed patient selection criteria have been previously published [2][3][4]. In addition to ensuring that there are no detectable metastases, good urinary function and predicted life expectancy of > 10years several new concepts have emerged:

i) Gland size: previous guidelines have recommended limits of 50-60ml however for both LDR and HDR, if there is minimal pubic arch interference, there is now published data showing that much larger glands can be successfully implanted with good results for both dosimetry and biochemical control with no excess toxicity. [5][6]

ii) Locally advanced prostate cancer (stage T3): There are now published data showing good oncological outcomes when stage T3a and T3b cancers are treated with either LDR or HDR brachytherapy boost [7][8].

iii) Outflow obstruction: with due attention to dose distribution patients having had previous intervention for outflow obstruction eg. Transurethral resection of prostate (TURP) or Holmium laser enucleation of the prostate (HoLEP), even where there is a significant residual cavity, can undergo LDR or HDR brachytherapy without an increase in risk of urinary toxicity.[9][10] Typically an interval of 3 to 6 months post-procedure is allowed.

iv) Prostatic calcification: it has been shown that calcifications in LDR brachytherapy result in cold spots within the implanted volume when using TG43 formalism and one study has shown a detriment in biochemical control with 10 year biochemical relapse free survival falling from 91.8% to 78.8% in patients with significant intraprostatic calcification.[11] However a more recent study using Cs-131 did not confirm this [12]. HDR uses higher energy and therefore calcifications have a clinically negligible impact on dosimetry.

Recommendations:

- Consider brachytherapy for prostate glands >60ml provided no pubic arch interference is likely

- T3 prostate cancer can be considered for brachytherapy in combination with external beam radiotherapy
- TURP and HoLEP are not a contraindications to brachytherapy
- HDR is preferred where there are extensive calcifications

Grade B, Level 2b

Prostate Brachytherapy Techniques

If not indicated otherwise the descriptions below apply both to LDR and HDR prostate brachytherapy. Modern prostate brachytherapy is a transperineal, transrectal ultrasound (TRUS) guided technique which has been well described previously [2][3][4]
Treatment planning for LDR and HDR prostate brachytherapy can be performed either using forward planning, graphical optimization, inverse planning, or by mixed approaches [13][14]. Typically TG43 formalism is used for LDR and HDR BT dose calculation.

LDR
The original two stage Seattle technique, although still used in a few departments has been largely replaced by single step techniques which avoid two procedures and the challenge of reproducing geometry from one step to the next. Adaptive real time planning enables modifications to be made during implantation to optimise the dose distribution. A review of these methods has been previously published [13].

HDR
Two approaches are used; a single step procedure which is based entirely on ultrasound and a two-step procedure in which transrectal ultrasound based implantation is followed by CT and/or MR imaging on which the treatment volume and planning are based. Neither approach has been shown to be superior with advantages and disadvantages to each.

Recommendations

- Single step adaptive implantation techniques are recommended for LDR brachytherapy
- TRUS based single step or CT/MR based two step techniques are acceptable for HDR brachytherapy

Grade D, Level 5

Target definitions (GTV and CTV)

Tumour and target definitions for LDR brachytherapy have been published [4]. Similar definitions are used for HDR brachytherapy.

The Gross Tumour Volume (GTV) is defined as visible tumour on imaging and can be identified from pre-biopsy multi-parametric- (mp) MRI, which combines anatomic T2-weighted (T2W) with functional diffusion-weighted imaging (DWI) and its derivative apparent-diffusion coefficient (ADC) maps, and physiological dynamic contrast-enhanced (DCE) imaging. Pathological correlation with mapping biopsy results is advised. CT PET using PSMA, choline or fluciclovine may complement this information. This is particularly valuable when considering a focal boost or salvage treatment.

The Clinical Target Volume (CTV) is defined by the capsule of the prostate gland for organ confined disease. In patients with locally advanced disease the CTV should also include any extra-capsular extension and/or seminal vesicle involvement. Some techniques define a two CTV concept, where CTV1 is defined as whole gland and CTV2 as peripheral prostate zone [14]. Defining the CTV is mandatory whilst GTV is optional depending on whether focal GTV boosts are to be considered and the availability of pre-biopsy mp-MR with robust image fusion techniques.

The probability of microscopic extracapsular disease, variations in imaging technique used and other inherent uncertainties in any brachytherapy process should be considered when defining the CTV and PTV. Whilst some published series have used no margin a 3-5mm margin in each direction constrained to the rectum posteriorly and the bladder neck cranially should be considered.

OAR definitions

These are detailed in previous guideline publications [2][3][4] and include the prostatic urethra and outer wall of the anterior rectum [12].
Other structures such as the bladder base or neck, penile bulb, and neurovascular bundles may also be included but currently no robust dose constraints have been published to make their definition mandatory.

Recommendations

- CTV and PTV for prostate brachytherapy is defined by the prostate capsule and any extraprostatic disease; an additional margin to the PTV to account for extracapsular microscopic disease, variations in imaging modalities and procedural uncertainties of 3-5mm may be considered constrained to the rectum posteriorly and the bladder neck cranially
- OARs for prostate brachytherapy are anterior rectal wall and prostatic urethra

Grade D, Level 5

Prescription and planning aims

Table 1 shows the planning aims and objectives of permanent brachytherapy using I-125, the most commonly used isotope [4]. In these guidelines relative volumes are given as criteria for dose to the urethra, despite the fact that absolute volume parameters are more constant and not subject to variations in contouring concepts[15]. Urethra $D_{0.1cc}$ has been proposed as more useful than urethra D_{10} and the usefulness of Urethra D_{30} when reporting the dose to the urethra has been questioned. Urethra V_{150} and V_{100} can also give additional information on the dose distribution over the urethra. However there is insufficient clinical validation of absolute parameters at present and therefore the planning aims and objectives as published in 2007 [4] are maintained in the present recommendations, but the absolute parameter $D_{0.1cc}$ for urethra should be reported.

For monotherapy the prescription dose to the CTV (equates to PTV) is 145Gy and for boost treatments after 45-50Gy external beam, 110Gy.

The use of seeds of uniform air kerma rate is recommended. Using seeds of different air kerma rates increases the risk of errors and complicates the post-implant dosimetry.

Table 1 Planning aims and objectives of permanent brachytherapy using I-125 and prescription dose of 145Gy (monotherapy).

Organ	Parameter	Objective
CTV	V_{100}	≥95%
	D_{90}	>145Gy
	V_{150}	≤60%
Rectum	D_{2cc}	≤145Gy
	$D_{0.1cc}$	<200Gy
Urethra	D_{10}	<150%
	D_{30}	<130%

Dose prescription and planning aims for HDR as boost and monotherapy are not as standardized as for LDR (table 2). The reasons for this are the different dose concepts and the variety of possible needle implant patterns, e.g. peripheral loading and uniform loading. However whilst several different multifractionation schedules have been reported, given the logistics of multifraction treatments and lack of evidence for superiority, the recommendation for a boost after 45-50Gy external beam is now a single dose of 15Gy. [16][17]

Table 2 Planning aims and objectives of temporary HDR brachytherapy

Organ	Parameter	Objective (*)	Objective for 15Gy brachytherapy boost only
CTV	V_{100}	>95%	>95% (14.3Gy)
	D_{90}	>100% (121Gy EQD2)	>100% (15Gy)
	V_{150}	≤40%	≤40% (6Gy)
Rectum	D_{2cc}	≤75Gy EQD2	≤10Gy
Urethra	D_{10}	≤120Gy EQD2	≤17Gy

	D_{30}	≤105Gy EQD2	≤15Gy

(*) EQD2 dose was calculated using the following concept: prescribed dose: external 25x2Gy, HDR brachytherapy 1x15Gy, α/β-ratio=1.5Gy, EQD2: 50Gy + 70.7Gy ≈ 121Gy.

Currently there is no evidence regarding the sequencing of boost treatments with the external beam radiotherapy component. Brachytherapy can be scheduled either before or after external beam depending on local policy and workflow.
In salvage brachytherapy there is no evidence for specific dose objectives. Some groups use the same doses as for primary treatment, others make modifications to a lower level with no comparative data on which to make a recommendation.

Recommendations

- For LDR I-125 monotherapy the prescription dose to the CTV is 145Gy and for boosts 110Gy.
- For HDR boosts the prescription dose to the CTV is 15Gy
- No evidence based recommendation for HDR monotherapy can yet be made.
- Brachytherapy boosts may be delivered before or after external beam treatment.

Grade B, Level 2b

Permanent Prostate Brachytherapy Quality Assurance

GEC-ESTRO ACROP recommendations on calibration and traceability of low energy LDR photon-emitting brachytherapy sources were published in 2020 giving guidelines on quality control of the radioactive sources [18] and GEC-ESTRO ACROP recommendations for quality assurance of ultrasound imaging in brachytherapy are available to explain practical test procedures and ensure high quality use of US [19]. Related practice guidelines to ensure high quality training and quality assurance have also been published [20][21][22].
Post implantation CT based dosimetry is generally recommended.[23][24] Post implant imaging can be undertaken day 1,2 or 2-6 weeks following the implant, but should always be done using the same timing as prostate swelling and consequent shrinkage could influence the results. A CT slice thickness of ≤3 mm is necessary [25, 26].
For post-implant dosimetry automatic seed finding tools can be used, but results should be evaluated carefully [25].
Post-implant dosimetry should measure the following parameters: Prostate $D_{90\%}$, $V_{100\%}$, $V_{150\%}$, and rectal dose (D_{2cc}). Without a catheter in situ urethra CT-based dosimetry is unreliable. Prostate delineation on CT can become very difficult due to scatter effects from the seeds. The use of MRI can improve the accuracy in delineating the prostate, but that way seed reconstruction becomes more difficult. In practice, combined modalities are often recommended: either MRI using a sequence for optimal prostate delineation and another sequence for better seed detection, or MRI for prostate delineation fused to a CT for seed reconstruction. Both options have their uncertainties and neither is optimal. Uncertainties resulting from image registration should also be considered [25].

Post-implantation results should be reviewed and action, such as re-implantation, considered for sub-optimal dosimetry in individual patients.
The impact on post-implant dosimetry of changes in personnel or implant technique should also be assessed by regular review, as a learning curve for permanent prostate brachytherapy is well described.

Temporary Prostate Brachytherapy Quality Assurance

Source calibration is an essential part of quality assurance in HDR BT. This has to follow national or international standards [27]
Of high importance is the catheter reconstruction, in particular the tip. Several techniques are published describing this issue. It can be image-based (CT or TRUS) or by measurement of the free length. The method used should fit workflow and the catheter tip should be evaluated shortly prior to the treatment. In particular when using one implant with multiple treatment fractions it must be checked that the positions have not changed between fractions [28].
In-vivo-dosimetry can be used to evaluate the correct applied dose. Nevertheless, with most in-vivo-dosimetry systems commercially available today only estimates can be made for doses e.g. in rectum and bladder [29], but developments look promising [30].

Recommendations

- Post LDR implant CT based dosimetry measuring prostate $D_{90\%}$, $V_{100\%}$, $V_{150\%}$ and rectal dose (D_{2cc}) should be undertaken at day 1,2 or 2-6 weeks after implantation
- Catheter tip position is important in HDR brachytherapy and should be checked before each fraction

Grade B, Level 2b

Monotherapy in localised prostate cancer

There are numerous series of LDR brachytherapy published, several with mature follow up. 10-year rates of freedom from biochemical failure (FFBF) are >85% with prostate cancer distant metastasis rates of <10% and prostate-cancer-specific mortality <5% in low risk patients with good outcomes including men <60yrs [31][32][33][34]. Grade 3-4 toxicity rates are consistently <4%.
Monotherapy using HDR temporary brachytherapy is less well established than with LDR permanent implants but overall results across comparable risk groups are no different. Optimal dose fractionation schedules are yet to be defined and have ranged from 4 or more fractions down to the current recommendation of two fractions delivering a total dose of 26-27Gy Single fraction schedules using 19Gy are associated with higher rates of biochemical failure across risk groups and are not recommended outside of clinical trials [35][36][37][38].

Recommendation

- Fractionated HDR monotherapy may be used for low and intermediate risk prostate cancer.

Grade B, Level 2a

Boost treatment with external beam radiotherapy in intermediate and high risk prostate cancer

For patients with unfavourable intermediate and high risk localised prostate cancer there is a significant risk of microscopic extra-capsular spread. In this situation brachytherapy may be combined with external beam radiotherapy as a dose escalation strategy to ensure an appropriate target volume is treated to high dose.

Unfavourable intermediate risk is defined as primary Gleason pattern of 4 (ISUP Grade group 3), and/or percentage of positive biopsy cores ≥50%, and/or multiple intermediate-risk factors (cT2b–c, PSA 10–20ng/mL, or ISUP Grade group 2/3) [39].

There are three randomised trials comparing external beam alone (EBRT) with a combined schedule of external beam and brachytherapy boost (EBRTBT) [40][41][42][43][44][45].

Dose-escalated external beam radiotherapy has been compared with external beam radiotherapy followed by a LDR brachytherapy boost in intermediate-risk and high-risk patients in the ASCENDE-RT (Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy) multi-centre Canadian trial [40]. Dose-escalated external beam radiotherapy (total dose of 78 Gy) was compared to external beam (total dose 46 Gy) followed by LDR brachytherapy boost (prescribed dose 115 Gy). In addition all patients received one year of androgen deprivation. With a median follow –up of 6.5 years a significant improvement in recurrence free survival at 7 years was found, increasing from 71% in the dose escalated external beam alone arm to 86% in the LDR boost arm. This was associated with a higher rate of late genito-urinary (GU) morbidity with a 5-year cumulative Grade 3 toxicity rate of 19% in the LDR boost arm compared to 5% in the external beam radiotherapy alone arm [43]. Approximately 50% of the GU toxicity was due to urethral strictures and it is recommended that a boost dose of 110Gy rather than 115Gy should be used. Care should also be taken not to over-treat the membranous urethra distal to the prostate apex when using this technique.

Conventional EBRT delivering 66Gy in 33 fractions has been compared with 40Gy in 20 fractions followed by a medium dose rate (1.2Gy/hour) iridium implant delivering 35Gy to the V100. [41][42]. No ADT was given in this relatively small study which included a total of 104 intermediate (40%) and high risk (60%) patients. Biochemical relapse free survival was 29% in the EBRT arm vs 61% in the EBRTBT arm but no difference in metastases free or overall survival was seen. The incidence of grade ≥3 GU toxicity at >18 months was higher in the EBRTBT arm (13.7%) vs 3.8% in the EBRT arm.

Modern high dose rate iridium afterloading brachytherapy has been evaluated in a randomised trial of hypofractionated EBRT (55Gy in 20 fractions) compared to a combined schedule of 35.7Gy in 13 fractions and HDR boost of 17Gy in 2 fractions [44][45]. 218 patients were entered, 40% intermediate and 55% high risk. ADT was received by 75%. With a minimum of 10 years follow up a significant advantage in favour of the EBRTBT for biochemical relapse free survival is seen (46% vs 39%)

but no difference in overall survival has emerged. There was no difference in GU toxicity, GI toxicity or quality of life between the two arms.

A meta-analysis including all three trials evaluating brachytherapy boost has confirmed a consistent advantage for biochemical control with a composite hazard ratio of 0.49 compared to external beam alone [46].

Recommendation

- HDR or LDR brachytherapy boost with external beam radiotherapy and ADT should be offered to patients with intermediate or high risk prostate cancer

Grade A, Level 1a

Comparative results of brachytherapy, external beam radiotherapy and prostatectomy

There is no randomised comparison between these three modalities. SPIRIT: Surgical Prostatectomy Versus Interstitial Radiation Intervention Trial was an attempt to randomise between brachytherapy and prostatectomy which only randomised 34 men but subsequently reported on 190 men who took part in an additional component based on treatment preference [47]. The only published result to date focuses on quality of life at median 5.2 years. There was an advantage for BT in urinary and sexual domains and in patient satisfaction.

There are a number of cohort studies comparing outcomes between modalities. A series of 2557 patients comparing LDR brachytherapy with external beam and surgery concluded that both LDR brachytherapy and radiotherapy achieved better biochemical control than surgery but other outcome parameters such as prostate specific and overall survival were the same [48]. LDR brachytherapy however had lowest rates of toxicity. The main difference between the treatment modalities relates to toxicities and this has been analysed in a systematic review of published data comparing surgery, EBRT and LDR or HDR monotherapy [49]. With up to 6 year follow up brachytherapy had the lowest rates of toxicity with transient urinary disturbance returning to baseline after one year whilst surgery had a negative impact on urinary and sexual function and EBRT had a negative impact on bowel function.

For combined external beam and brachytherapy, the largest multicentre study included 1809 men with Gleason 9-10 prostate cancer who received prostatectomy, EBRT alone or EBRTBT [50]. The combined brachytherapy cohort had significantly lower prostate cancer-specific mortality (HR 0.38 vs surgery and 0.41vs EBRT alone). However other studies have shown a less striking difference or even a benefit for surgery. A recently published NCDB analysis of 13,985 men (of whom 12,283 underwent surgery) reported with a median follow up of 91 and 101 months a hazard ratio of 1.22 in favour of prostatectomy [51].

These contrasting results reflect the inherent uncertainties and bias in cohort studies and lead to the conclusion that overall there is little difference in survival rates between the three modalities. Consistently however differences in toxicity profile are reported with surgery more likely to cause urinary and sexual function deterioration whilst irritative and obstructive urinary symptoms are more common with brachytherapy, particularly in the first two to three years after implant.

Recommendation

- Brachytherapy, external beam, and prostatectomy are all effective treatments for organ confined prostate cancer
- Irritative and obstructive urinary symptoms are more common after brachytherapy but overall urinary and sexual function is better than after surgery.

Grade B, Level 2a

Role of Androgen Deprivation Therapy (ADT) with prostate brachytherapy

ADT provides effective prostate volume reduction and can be used for pre-treatment downsizing to avoid pubic arch interference during the implant procedure. Volume reduction of around one third is achieved using 3 months of neo-adjuvant LHRH antagonists, LHRH agonists or a combination of bicalutamide and dutasteride [52].

In patients with low and favourable intermediate risk prostate cancer treated with brachytherapy as monotherapy, systematic review demonstrates no clinical or biochemical control benefit from the addition of ADT to brachytherapy [53]. Care should be taken when using ADT in older men and those with pre-existing cardiac co-morbidity as decreases in overall survival are likely because increased ADT-associated cardiac mortality has been noted in retrospective studies [54].

In patients with intermediate and high risk prostate cancer undergoing EBRT alone, the addition of ADT has demonstrated improved local control, biochemical disease free survival, metastases free survival, and overall survival in multiple randomised controlled trials (RCTs) [55]. The addition of ADT to EBRT appears to both improve local control and eradicate subclinical micro-metastatic disease.
Radiation dose escalation using EBRT results in improved biochemical control with some limited data showing as a reduced rate of metastases and one trial comparing 70Gy with 78Gy reporting at 15 years a 3% reduction in prostate specific mortality [56][57].

Radiation dose escalation using a brachytherapy boost in addition to EBRT provides much higher biological doses (for HDR BED $\geq$ 215 Gy, α/β=1.2 Gy) but currently there are no prospective randomised data to support the omission of ADT in these patients where ADT use independently predicts better outcomes regardless of dose intensification [53][58][59].

Omitting ADT in unfavourable intermediate and high risk patients undergoing brachytherapy boost with EBRT may result in inferior overall survival and based on current evidence ADT use and duration should be in line with that used when delivering EBRT alone.

Recommendation

- ADT should be used in addition to brachytherapy in line with that used when delivering EBRT alone for unfavourable intermediate risk and high risk patients

Grade B, Level 2a

Second malignancy after prostate brachytherapy

Second malignancy risk after EBRT is well recognized with a risk of up to 1 in 70 after 10 years or more of follow up [60]. In contrast both LDR and HDR brachytherapy monotherapy result in low estimated risks of radiation-induced second malignancy. In particular excess absolute risks for LDR brachytherapy of 0.71 per 10,000 person-years (PY) and 0.84 per 10,000 PY respectively for rectal and bladder cancer have been estimated [61]. The corresponding rates for HDR brachytherapy were 0.74 and 1.62 per 10,000 PY respectively.

Focal and focal boost Brachytherapy

Focal therapy, where only gross tumour or hemi-gland is treated, has been promoted in localised prostate cancer aiming to reduce the morbidity seen with radical therapy, whilst maintaining cancer control. There are a number of competing modalities which have been used to explore focal therapy including cryotherapy, high frequency ultrasound, electroporation, EBRT and brachytherapy. A review of published data on brachytherapy identified 9 dosimetry papers all of which showed equivalent or increased dose to the GTV and lower doses to the OAR is feasible [62]. In six small clinical studies which included a mean of 7 patients (range 1-20) and a mean follow up of 23 months each, two reported high biochemical relapse rates of 28% and 15% although toxicity was very low. The POWER study (Netherlands Trial Register NL7073) [63] aims to evaluate whether hemi-gland brachytherapy will result in less erectile dysfunction when compared to whole gland brachytherapy in patients with unilateral significant adenocarcinoma of the prostate. Currently focal brachytherapy is only recommended within the context of a clinical trial.
It is also possible to use a focal boost to the GTV when brachytherapy is delivered to the whole gland. One dosimetric study [64] shows that with HDR an increase in dose to the focal PTV to 21Gy is feasible with a 15Gy whole gland prescription within planning dose constraints for OARs. However, a prospective series of 60 patients treated with HDR brachytherapy alone delivering 19Gy to the whole gland and a boost to the dominant intraprostatic lesion of ≥23Gy showed no benefit from the dose escalation with 7 of 8 biopsy proven recurrences in the boost volume.[65] Further evaluation of the utility of this approach with different doses is warranted but currently it is only recommended within the context of a clinical trial.

Recommendation

- Focal and focal boost brachytherapy are only recommended within the context of a clinical trial.

Grade C, Level 4

Salvage Brachytherapy following previous radiation

Isolated local recurrence of prostate cancer following primary radiotherapy or brachytherapy may be treated with salvage brachytherapy, using either LDR or HDR, and treating whole or partial gland volumes. Patient selection for salvage is an important issue with no firm consensus with regard to presenting parameters, interval

to relapse or risk parameters (PSA, stage and grade) at relapse [66]. Exclusion of metastatic disease is critical but represents a major challenge. Despite modern imaging including PSMA PET in most published series, around 50% of patients relapse with regional or distant disease. Reirradiation of the whole gland and focal reirradiation to radiologically or histologically proven segments of relapse are both reported. In a recent review of 11 published series using HDR brachytherapy containing between 7 and 113 patients dose fractionation schedules vary from 19 Gy in 1 fraction to 42 Gy in 6 fractions and five year biochemical control rates were between 18 to 77%. [67] Late grade 3 genitourinary toxicity was seen in up to 32% and gastrointestinal toxicity was up to 5.1%.
A review of 4 small series (7-20 patients) using low dose rate brachytherapy for salvage delivering 144-145Gy reports early (2 to 3 year) biochemical relapse free rates of 58-78% with very few toxicity events [68].

- In a recent systematic review and meta-analysis of local salvage therapies including stereotactic body radiotherapy (SBRT), LDR and HDR brachytherapy and prostatectomy there was no difference in 5 year recurrence free survival in the radiation modalities at 60%. More severe lower GU toxicity was seen with prostatectomy; 20% compared to 9.6% and 9.1% after LDR and HDR brachytherapy respectively. HDR brachytherapy resulted in the lowest severe GI toxicity with 0% reported[69].

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.

Recommendation

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

Grade C, Level 4

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