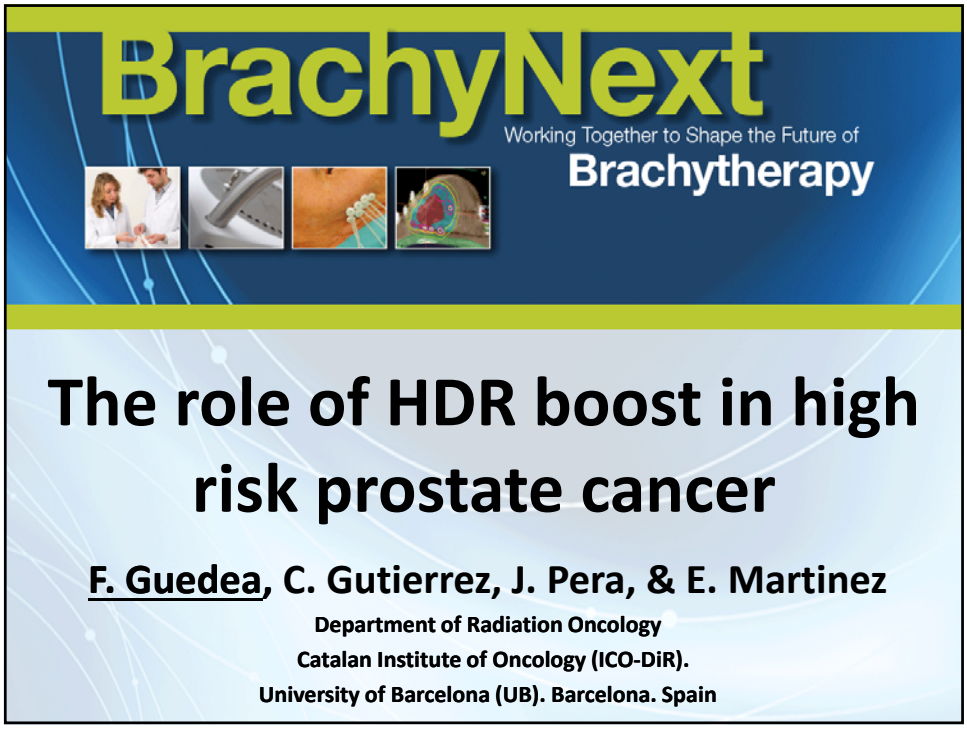

The role of HDR boost in high risk prostate cancer

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Department of Radiation Oncology
Catalan Institute of Oncology (ICO-DiR).
University of Barcelona (UB). Barcelona. Spain

Disclosures

Non-salaried Consultant for Nucletron.

I have received honoraria for lectures from Varian & Zeiss.

Outline of the presentation

- Potential advantages of BT in front of new technologies for EBRT (SBRT, VMAT, ..) in prostate cancer & evolution of prostate BT:
- Potential advantages of HDR in front of LDR implants in prostate cancer & Guidelines for HDR BT:
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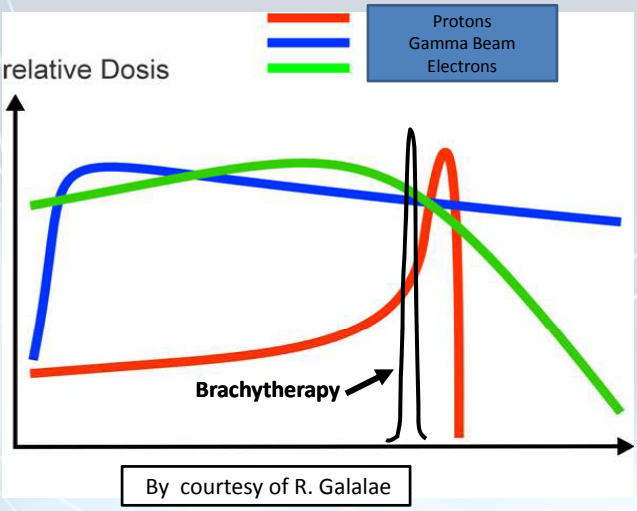
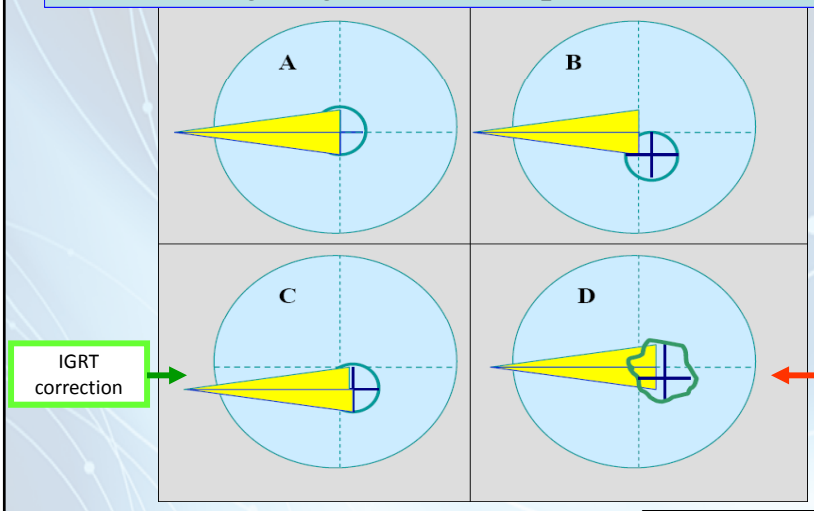
- Literature review for phase II trials for High Risk Prostate Cancer with HDR monotherapy:
- Catalan Institute of Oncology experience:
- Conclusions:

Potential of Brachytherapy: IntegraI dose very low



By courtesy of R. Galalae

Potential of Brachytherapy:
Moving target is not a problem in BT
Moving target remains a problem in EBRT

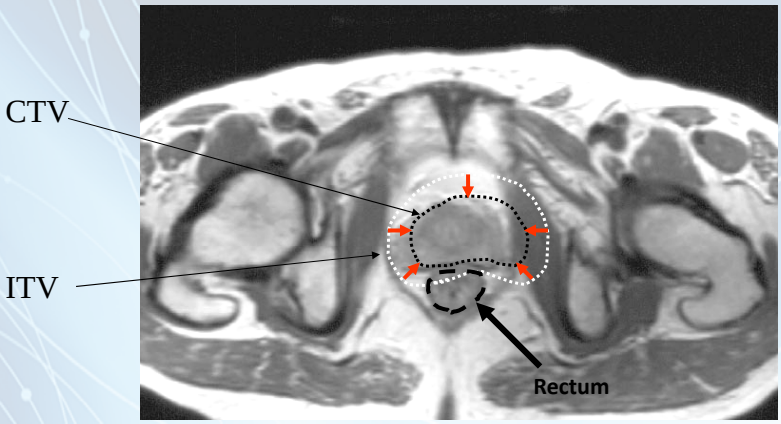


By courtesy of R. Galalae

Potential of Brachytherapy:
Moving target is not a problem in BT
Moving target remains a problem in EBRT

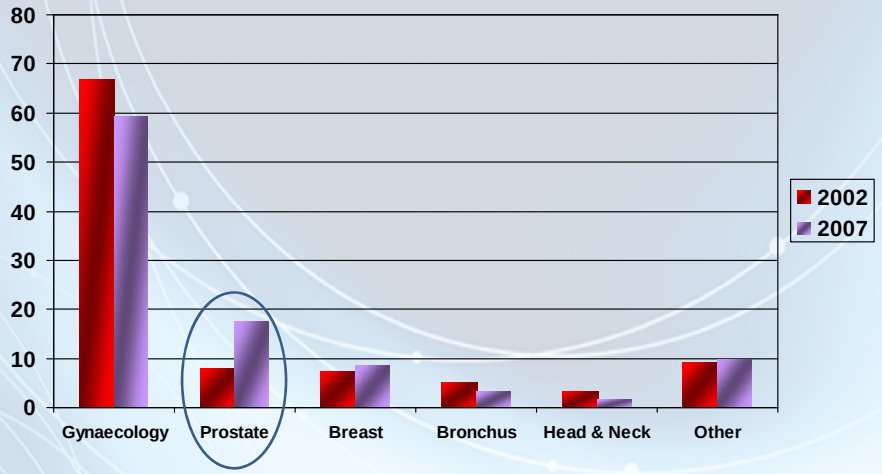
Interstitial Brachytherapy for Prostate: CTV = PTV

No margin necessary . Much smaller PTV



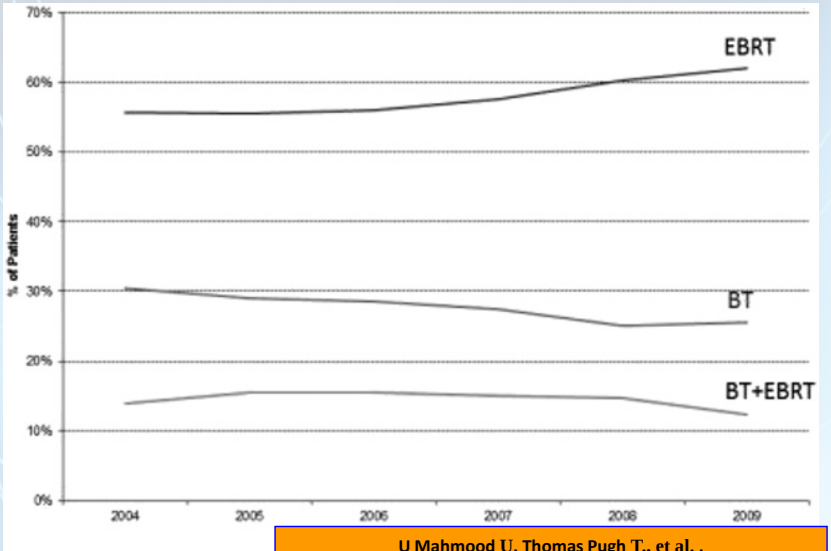
By courtesy of R. Galalae

Evolution of prostate BT from 2002 to 2007 in Europe: PCBE survey



Guedea F., Venselaar J., Hoskin P., et al.,
Radiot. and Oncol. 97. 514-520. 2014.
Patterns of care for BT in Europe: Updated results.

Evolution of prostate BT from 2004 to 2009 in USA



U Mahmood U, Thomas Pugh T., et al. ,
Declining use of brachytherapy for the treatment of prostate cancer.
Brachytherapy 13. 157-162 . 2014.

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Comparation of HDR & LDR implants

	High-dose-rate	Low-dose-rate
Conformal treatment	++++	++++
Target accuracy	++++	++++
Ability to treat extracapsular extension	++++	+
Ability to treat seminal vesicles	++++	++
Ease of control of radiation	++++	++
Lack of cold/hot spots	++++	++
Control of critical organ dose	++++	++
Modify dose distribution	++++	+
Need for external beam	Yes/Sometimes	No/Sometimes
Monotherapy	+	+++
Experience of physician	Crucial	Crucial
Pre-planning dosimetry	Not needed	Extensive (TRUS)
Post implant dosimetry	Not needed	Extensive (CT)
Stages treated	All, T1-T3	T1-T2
Gland volume > 60 cc at time of implant	Less difficulty	More difficulty
Pubic arch interference at time of implant	Less of a problem	Can't be done
Prior TURP	Less of a problem	Can't always be done
Final Dose Verification	Pre-treatment	Post treatment
Symptom duration	Weeks	Months

Skowronek J (Poland)
J Contempary Brachytherapy. 2013;5(1):33-41. LDR or HDR in treatment of prostate cancer

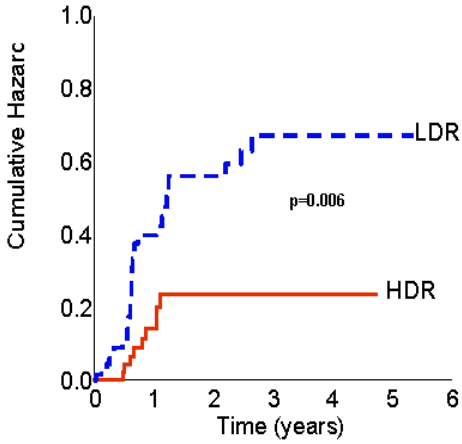
Erectile Dysfunction: HDR vs LDR (Pd103)

In a series of 330 pts from the Beaumont Hospital, monotherapy with HDR (4-6 fractions, 38-42 Gy, twice a day) has the same 4-year biochemical control that with LDR (97,5%).

The 4-y ED was 18,3% for HDR and 41,3% for LDR (p=0,006)

Martinez A., Ghilezan M., et al.,
Radiot. and Oncol. 71 (Supplement 2), S28, S52, S56, 2004.
Brachytherapy in prostate cancer: HDR vs LDR (Pd 103),
Results, Chronic toxiciy, Erectile Dysfunction (ER)

Erectile Dysfunction: HDR vs LDR (Pd103)



Martinez A., Ghilezan M., et al.,
Radiot. and Oncol. 71 (Supplement 2), S28, S52, S56, 2004.
Brachytherapy in prostate cancer: HDR vs LDR (Pd 103),
Results, Chronic toxiciy, Erectile Dysfunction (ER)

In prostate BT, other HDR advantages over seeds

- Ability to treat extracapsular extension.
- Ability to treat bigger prostate volumes.
- Ability to treat Seminal vesicles.
- Ability to treat all stages (T1-T3).
- Shorter duration of symptoms after procedure.

Guidelines for HDR BT in prostate cancer

Author	Journal & Year	Title
Kovacs et al.	Rad & Oncol. 2005.	GEC-ESTRO recommendations
Wojcieszek P., et al.	J Contemp BT. 2012.	guidelines overview
Yamada Y., et al.	Brachytherapy. 2012.	ABS Guidelines
Hoskin P., et al.	Rad & Oncol. 2013.	GEC/ESTRO recommendations: update
Hsu I., et al.	Brachytherapy. 2014.	ACR Guidelines

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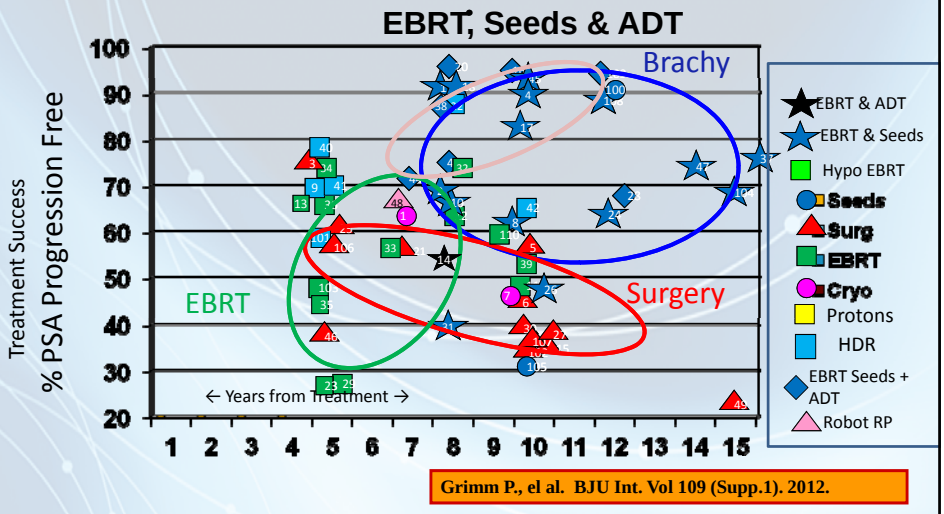
- Conclusions:

High Risk Prostate Cancer results over 18000 papers identified during 2000 to 2010



Grimm P., el al. BJU Int. Vol 109 (Supp.1). 2012.

Boost with HDR in IR & HR Prostate cancer:

Author	No. of patients	Median FU (months)	bNED (%)
Eulau (2000)	104	78	77
Pellizzon (2003)	119	41	75
Martin (2003)	102	31	82
Martinez (2003)	507	56	74
Galalae (2004)	611	60	77 (5y), 73 (10y)
Ares (2009)	77	50	87
Agoston (2011)	100	61	84,2 (IR) & 81,6 (HR)
Prada (2012)	313	71	79

Boost with HDR in high risk prostate cancer: Results of a multicentric study

	611 patients
Center	
Beaumont Hospital (USA)	309
Seattle (USA)	104
Kiel University (Germany)	198
Median FU: 5 years	
bDFS at 5y: 77%	bDFS at 10y: 73%

Boost with HDR in IR & HR:

- **Methods and Materials:** 280 pts have been treated with 60 Gy EBRT + HDR-BT boost for intermediate to high-risk prostate cancer (10 Gy). Among these, the outcome and toxicity of the first 100 patients treated with a single HDR-BT fraction were assessed.
- **Results:** Median FU was 61.5 months. 5y OS, cause-specific survival, disease-free survival, & bNED were 93.3%, 99.0%, 89.3%, and 85.5%, respectively. The 7-year actuarial rate of bNED was 84.2% for the intermediate risk and 81.6% for the high-risk
- **Conclusions:** 5y. outcome after 60Gy EBRT plus a single fraction of 10Gy HDR-BT boost is encouraging.

Ágoston P, Major T, Lövey J, Polgár C, et al. (Hungary)
Brachytherapy. 2011;10:376-84.
Moderate dose escalation with single-fraction HDR-BT boost for clinically localized intermediate- and high-risk prostate cancer: 5-year outcome of the first 100 consecutively treated patients

Boost with HDR in IR & HR:

- **Patients and Methods:** 313 patients with localized prostate cancer were treated with 46 Gy of EBRT to the pelvis with a HDR-BT boost. The median FU was 71 months
- **Results:** The 10-year actuarial biochemical control was 100% for patients with no high-risk criteria, 88% for patients with two intermediate-risk criteria, 91% with one high-risk criterion and 79% for patients with two to three high-risk criteria (P=0.004). The 10-year cancer-specific survival was 97%

Prada PJ, González H, et al (Spain)
BJU Int 2012 Jun;109(12):1787-93
Biochemical outcome after HDR intensity modulated brachytherapy with EBRT: 12 years of experience

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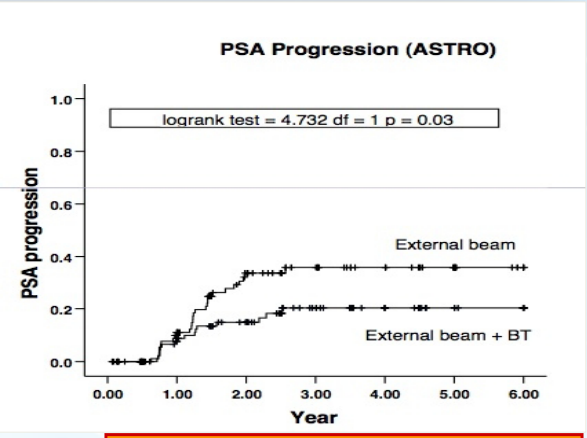
- Catalan Institute of Oncology experience:
- Conclusions:

Results of a phase III trial of 220 pts (T1-T3): Moderate Hipofractionated EBRT (20 x 2,75 Gy) vs Moderate Hypofractionated EBRT (13 x 2,75 Gy) + HDR boost (2x8,5 Gy)

For high & intermediate risk a reduction of 31% of recurrence & similar toxicity in both arms.



Hoskin P., el al. Rad & Oncol. 114-120. 2007.

Hoskin P., el al. Rad & Oncol. 217-222. 2012.

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Monotherapy with HDR in LR, IR & HR:

	n	Median follow-up (months)	Biochemical disease-free survival by risk group			High dose rate dose/fraction
			Low	Intermediate	High	
Shah 2012	252	58	91%	75%		38 Gy/4
Hoskin 2012	25	60				36 Gy/4
	30	54		95%	87%	34 Gy/4
	109	34				31.5 Gy/3
	33	6				26 Gy/2
Prada 2012	40	19	100%	88%		19 Gy/1
Rogers 2012	284	32		94%		39 Gy/6 (2 implants)
Zamblogou 2013	718	53	95%	93%	93%	39 Gy/4 – 34.5 Gy/3
Barkati 2012	79	40	89%	78%		30 Gy, 31.5 Gy, 33 Gy, 34.5 Gy/3
Yoshioka 2011	112	65	85%	93%	79%	54 Gy/9
Demanes 2011	298	62	97%			42 Gy/6 (2 implants) or 38 Gy/4

Morton G., & Hoskin P, Clinical Oncology 2013

Monotherapy with HDR in IR & HR:

- **Material & Methods: A total of 197 patients were treated with 34 Gy in four fractions, 36 Gy in four fractions, 31.5 Gy in three fractions, or 26 Gy in two fractions. Median FU was 60, 54, 36, and 6 months.**
- **Results: At 3 years, 99% of patients with intermediate-risk and 91% with high-risk disease were free of biochemical relapse (p= 0.02).**
- **Conclusions: There was no significant difference in urinary and rectal morbidity between schedules. Biochemical control of disease in patients with intermediate and high risk of relapse was good.**

Hoskin P, et al (UK)
Int J Radiat Oncol Biol Phys. 2012;82(4):1376-84.
HDR brachytherapy alone for localized prostate cancer
in patients at moderate or high risk of biochemical recurrence

Monotherapy with HDR in LR, IR & HR:

- **Methods and Materials: Between 2002 &2009, 718 pts with localized prostate cancer were treated with HDR monotherapy. 3 treatment protocols were applied; 141 patients received 38.0 Gy using one implant in 4 fractions of 9.5 Gy; 351 patients received 38.0 Gy in 4 fractions of 9.5 Gy, using 2 implants (2 weeks apart) and 226 patients received 34.5 Gy, using 3 single-fraction implants of 11.5 Gy (3 weeks apart).**
- **Results: Median FU was 52.8 months. The 36, 60, & 96 month biochemical control and metastasis-free survival rates were 97%, 94%, and 90% and 99%, 98%, & 97%.**
- **Conclusion: HDR monotherapy is safe & effective.**

Zambologlou N, Baltas D, Martin T, et al (Germany)
Int J Radiat Oncol Biol Phys. 2013;85(3):672-8
HDR interstitial brachytherapy as monotherapy for clinically localized prostate cancer: treatment evolution and mature results

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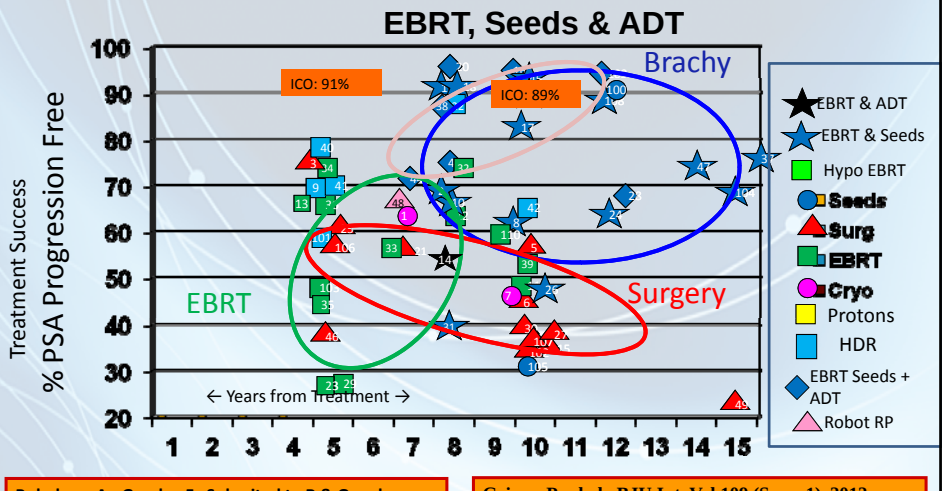
- Conclusions:

Results of 377 pts with High Risk Prostate cancer treated with EBRT (60 Gy) + HDR-BT (9 Gy) + AD 3y at ICO. Median FU: 48,7 months.



Boladeras A., Guedea F., Submited to R & Oncol.

Grimm P., el al. BJU Int. Vol 109 (Supp.1). 2012.

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- Conclusions:

Outline of my presentation

1. HDR-BT is more cost effective than seeds.
2. Results for HDR boost in high risk patients are excellent & well established (with one Phase III trial).
3. Results for HDR monotherapy in LR, IR & HR are promising.
4. HDR Prostate BT is gaining in popularity.
5. HDR Prostate BT is getting more widely used.

Modified from Skowronek J (Poland)
J Contempary Brachytherapy. 2013;5(1):33-41
Low-dose-rate or high-dose-rate brachytherapy in treatment of prostate cancer – between options