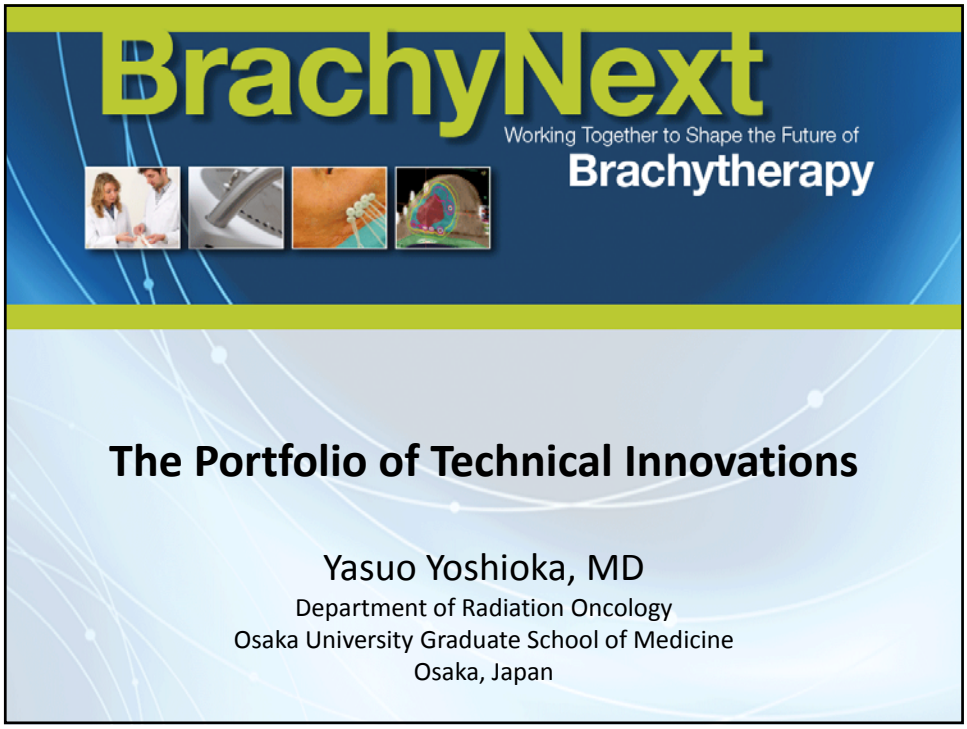


The Portfolio of Technical Innovations

Yasuo Yoshioka, MD
Department of Radiation Oncology
Osaka University Graduate School of Medicine
Osaka, Japan

Disclosure

Yasuo Yoshioka, MD, does not have any financial relationships or products or devices with any commercial interest related to the content of this activity of any amount during the past 12 months.

To Which Site Have We Applied HDR Brachytherapy? (Osaka Univ.)

Tongue

Floor of Mouth, Lip

Oropharynx

Esophagus, Bronchus, Bile duct, Intravessel

Breast (boost, APBI)

Primary uterine cervix (and corpus) cancer,

Recurrent cervix and corpus cancer

Prostate

Recurrent rectal cancer

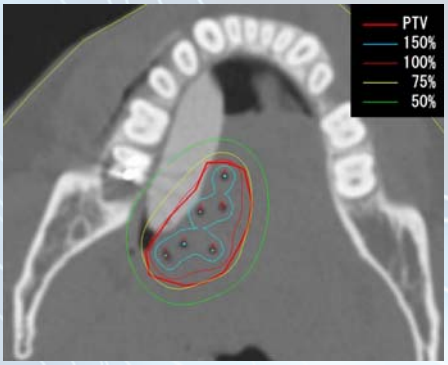
Soft tissue

We installed this type of HDR unit in 1991, as the first in Japan. We treated over 1,000 patients over 20 years.

High-Dose-Rate (HDR) Interstitial Brachytherapy for Oral Cavity Cancer

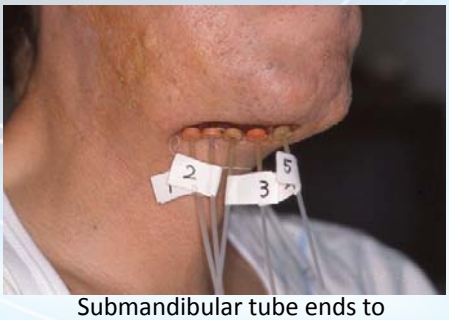
- Technique
- Clinical results
- Discussion, criticism, recommendations

Single-plane tubing
in HDR brachytherapy
for border of tongue cancer

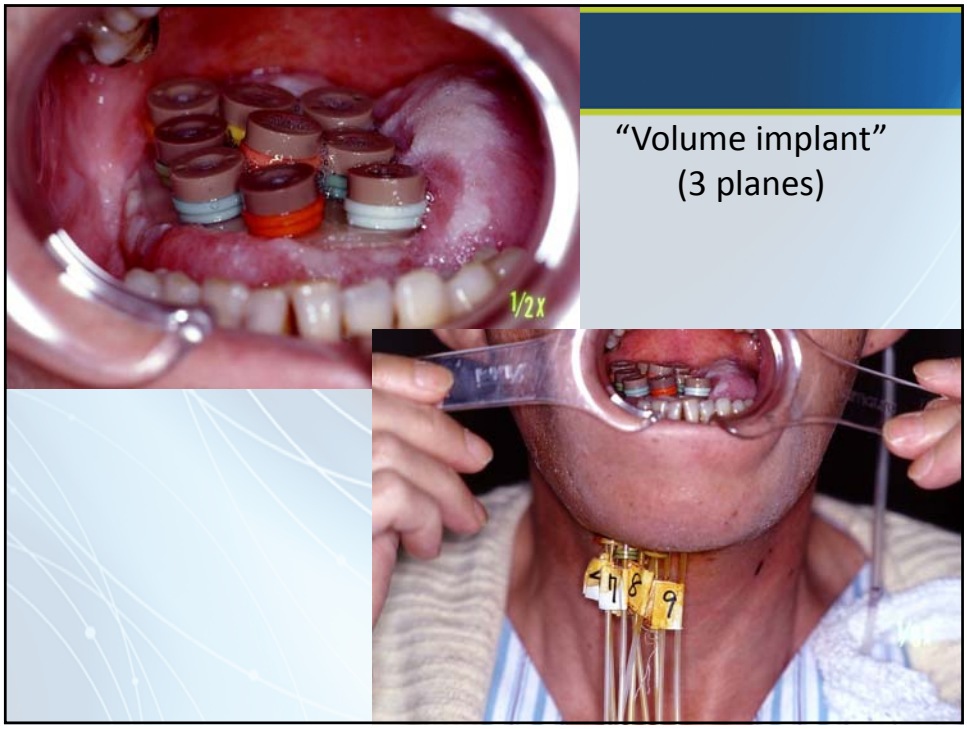


Dwell-times optimized.
Dose to mandible <50% due to spacer

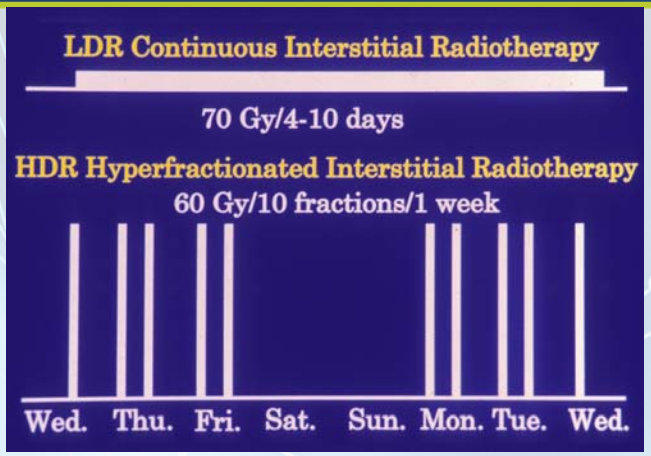
Spacer inserted in each irradiation
to protect lower gum



Submandibular tube ends to
be connected to HDR unit



Our Phase I/II Study Showed: LDR 70 Gy = HDR 60 Gy/10 Fr/7 d

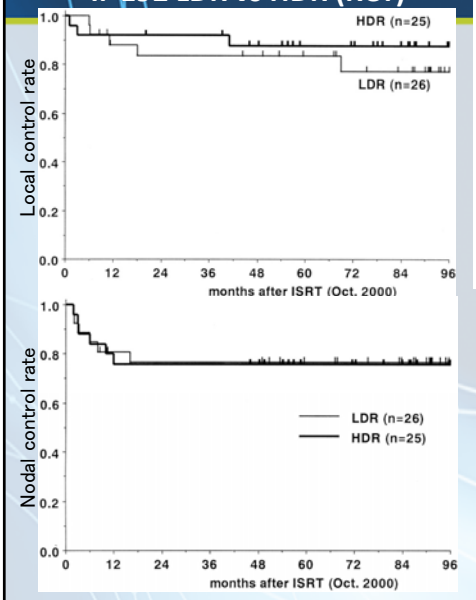


(Slide by T. Inoue)

LDR (^{192}Ir hair pins): patients isolated in sealed room for 4-10 days (according to the activity of ^{192}Ir).

HDR (^{192}Ir stepping source): No need to isolate patients, no radiation exposure to staff. Dwell time optimization--homogeneous distribution, short irradiation time keeps dosimetry.

T1-2 Oral Tongue Cancer Ir-192 LDR vs HDR (RCT)



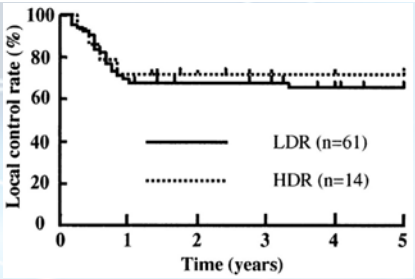
Inoue T, et al. Int J Radiat Oncol Biol Phys, 2001

Toxicity after brachytherapy for T1-2 tongue Ir-192 LDR vs HDR (RCT)

	LDR	HDR
N	26	25
Local failure	5	3
Ulcer	1	1
Bone exposure	0	2*

*Both patients with inadequate or no spacer

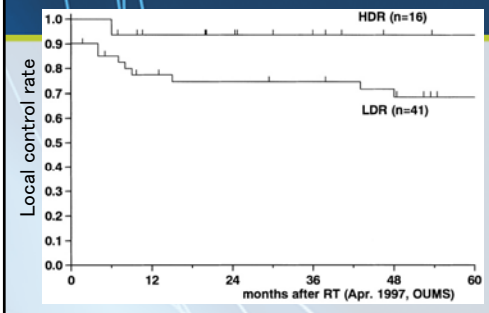
T3 oral tongue cancer Ir-192 LDR vs HDR (non-RCT)



Kakimoto N, et al. Radiother Oncol, 2003

HDR Brachytherapy for Mouth Floor

Mouth Floor Cancer: HDR ^{192}Ir vs LDR ^{198}Au



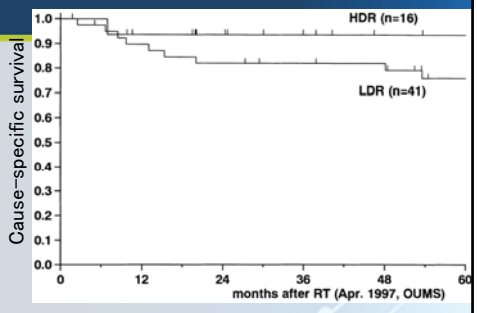
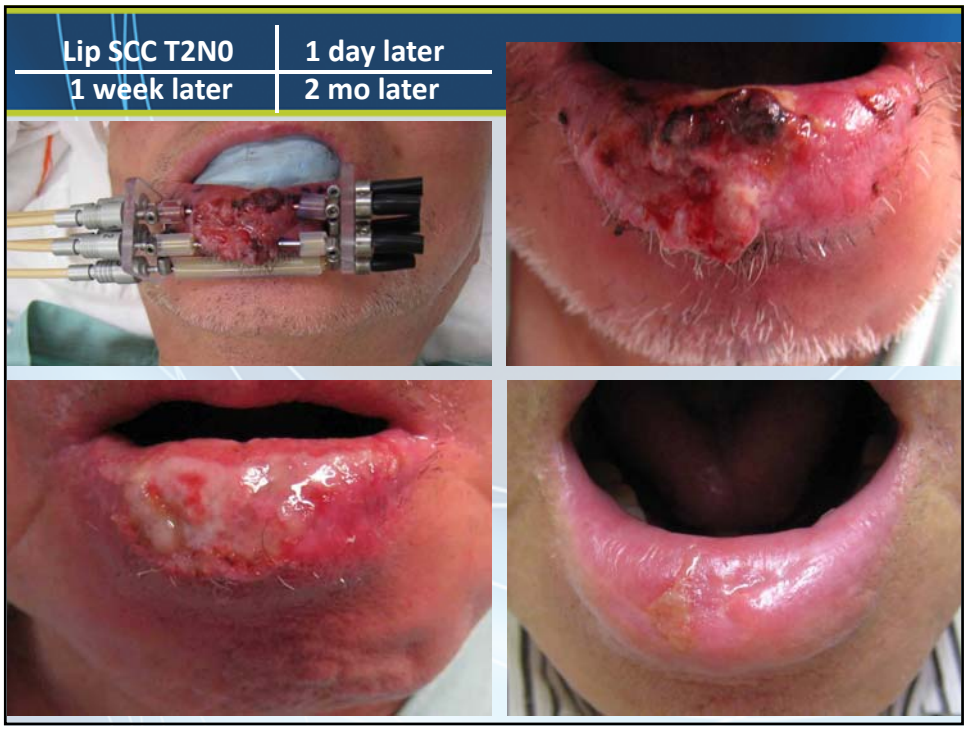


Table 7. Bone exposure and/or ulcer by dwell length

Source	Lower gum invasion	Dwell length (mm)	No. patients	Bone exposure and/or ulcer
HDR	+		5	3
	−	≤ 15	6	0
		≥ 20	5	3
	Total		16	6 (38%)
LDR	+		6	3
	−		35	10
	Total		41	13 (32%)

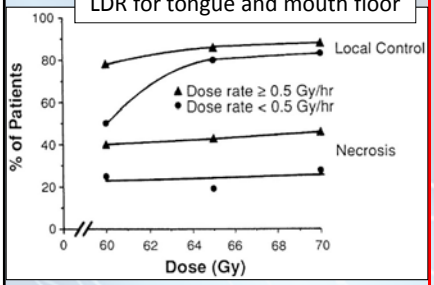
Inoue T, et al.
Int J Radiat Oncol
Biol Phys, 1998



Dose Rate Effect

Necrosis is dose-rate dependent,
Local control is total-dose dependent
↓
Normal tissue has a dose rate effect,
whereas tumor has not (or little).

LDR for tongue and mouth floor



Note: just comparison within LDR.
Not HDR vs LDR.

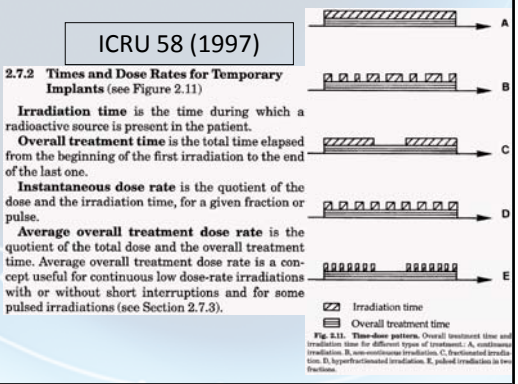
Mazeron JJ, et al.
Radiother Oncol 21:39-47,1991,
modified by Hall EJ

Is Dose Rate of HDR Really High?

ICRU 38 (1985)

LDR: 0.4-2 Gy/h
HDR: >12 Gy/h

ICRU 58 (1997)



Average overall treatment dose rate: HDR = LDR?!
54 Gy/9 fr/5 d (OTT = 4 d) = 0.56 Gy/h (LDR!)
60 Gy/10 fr/7d (OTT = 6.75 d) = 0.37 Gy/h (LDR!)

GEC-ESTRO recommendations

GEC-ESTRO recommendations for brachytherapy for head and neck squamous cell carcinomas

Jean-Jacques Mazeron [a,*], Jean-Michel Ardiet [b], Christine Haie-Méder [c], György Kovács [d], Peter Levendag [e], Didier Peiffert [f], Alfredo Polo [g], Angels Rovirosa [h], Vratislav Strnad [i]

Radiother Oncol 91:150-6,2009

Dose and dose rate prescription

The recommended dose (LDR-PDR) is 65–75 Gy for the treatment with definitive brachytherapy and 25–30 Gy after 40–45 Gy of external beam radiotherapy [18]. If delivered postoperatively, these doses are reduced to 50–60 Gy and 10–24 Gy, respectively [19]. For salvage implants in a previously irradiated territory, a dose of 60 Gy is adequate. The recommended dose rate/pulse dose is .03–.07 Gy/h/24 h. The results of HDR brachytherapy remain to be validated in prospective studies. If it is the only technique available but not included in a prospective study, treatment should be delivered in fractions of less than 3–4 Gy [20].

The use of the linear-quadratic model is recommended to calculate iso-effective fractionation schedules, with alpha beta value of 10 Gy and half time of repair of 1.5 h [12].

Mobile tongue

In general, in LDR brachytherapy, delivering a high total dose is recommended to secure local control, and to maintain the dose rate between 0.3 and 0.6 Gy/h in order to minimize late side effects [7,8]. With HDR brachytherapy, a smaller dose per fraction may reduce tissue injury, but a higher number of fractions are required. Doses between 3 and 4 Gy per fraction have been recommended [9]. When irradiation is delivered twice a day, the interval between fractions should be as long as possible, with a minimum of 6 h. With PDR brachytherapy, which offers the biological advantages of LDR brachytherapy with the technological advantages of the HDR-afterloading method, daytime PDR schedules were introduced by

CLINICAL INVESTIGATION Head and Neck

THE AMERICAN BRACHYTHERAPY SOCIETY RECOMMENDATIONS FOR HIGH-DOSE-RATE BRACHYTHERAPY FOR HEAD-AND-NECK CARCINOMA

SUBIR NAG, M.D.,* ELMER R. CANO, M.D.,† D. JEFFREY DEMANES, M.D.,‡ AJMEL A. PUTHAWALA, M.D.,§ AND BHADRASAIN VIKRAM, M.D.,‖ FOR THE AMERICAN BRACHYTHERAPY SOCIETY

*Department of Radiation Oncology, Ohio State University, Columbus, OH; †Department of Radiation Oncology, Presbyterian University Hospital, Pittsburg, PA; ‡Department of Radiation Oncology, The California Endocurietherapy Cancer Center, Oakland, CA; §Department of Radiation Oncology, Long Beach Memorial Medical Center, Long Beach, CA; ‖Department of Radiation Oncology, Montefiore Medical Center, Bronx, NY

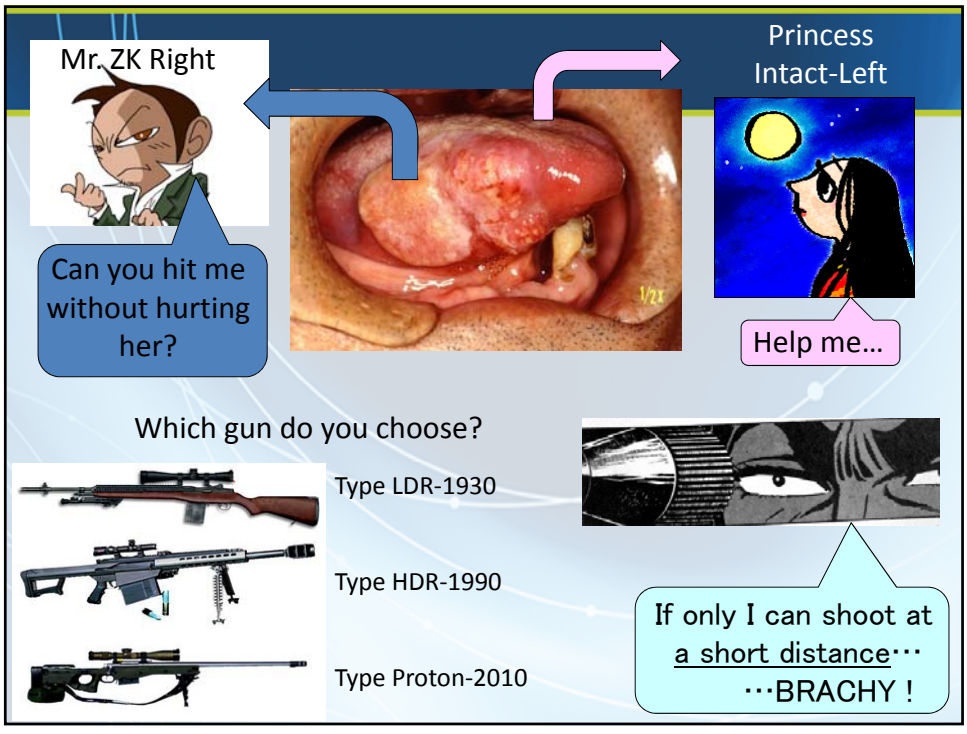
Int J Radiat Oncol Biol Phys 50:1190-8,2001

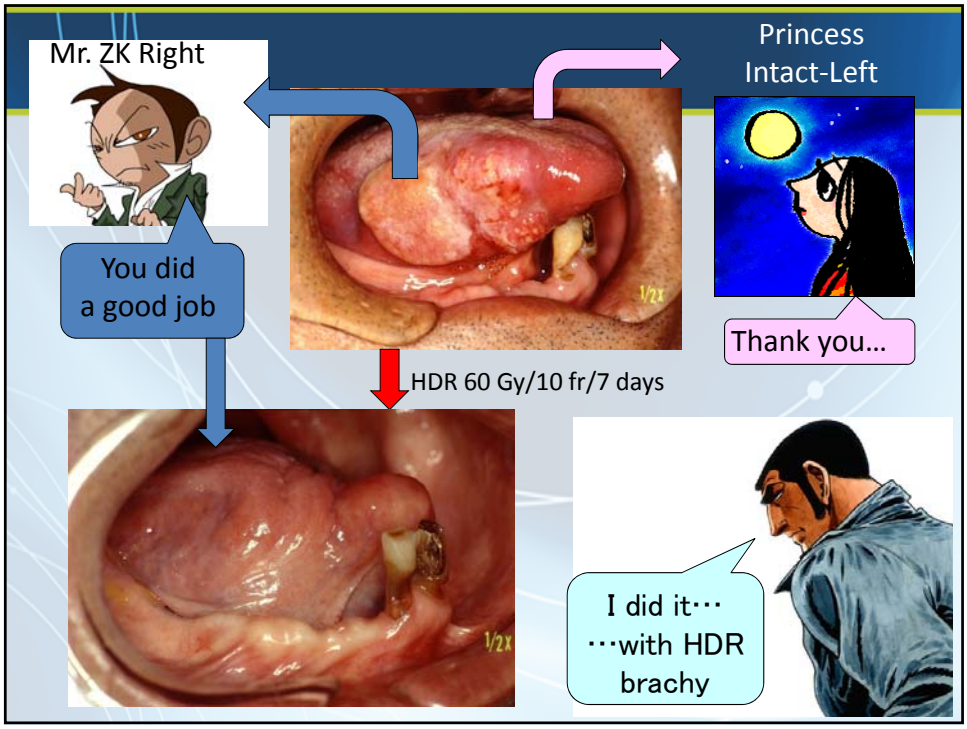
Table 1. Brachytherapy as sole treatment for oral cavity cancers

Author (ref)	EBRT	Fx Size (Gy)	# fx	Equiv. dose* (Gy)	# Pts.	L.C.
Dixit *et al.* (8)	0	3	20	65	3	–
Lau *et al.* (11)	0	6.5	7	63	27	53%
Inoue *et al.* (10)	0	6	10	80	14	100%
Donath *et al.* (9)	0	4.5–5	10	54–63	13	90%
Leung *et al.* (12)	0	5.5–6	10	71–80	13	100%

Abbreviations: Fx = fractions; equiv. = equivalent; Pts. = patients; L.C. = local control. EBRT = external beam radiation therapy.
* Equivalent dose for tumor effects as if given at 2 Gy/day using the linear quadratic model with an α/β ratio of 10 (25). See appendix.

(8–12). There is insufficient clinical information available to give firm treatment recommendations, but some ABS panel members had concern about the potential morbidity with fraction sizes as large as 6 Gy to the oral cavity.

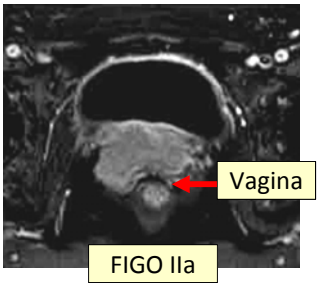




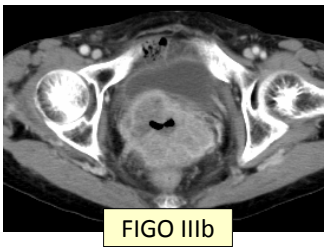
Uterine Cervix Cancer

Interstitial brachytherapy approach
to
Previously untreated
and
Previously treated (especially with prior RT)
Cervical cancer

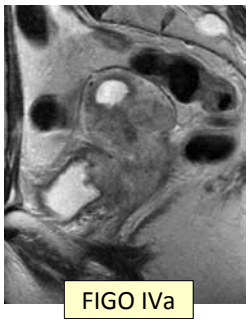
How Do You Treat Too Bulky or Extremely Deviated Cervical Cancer?



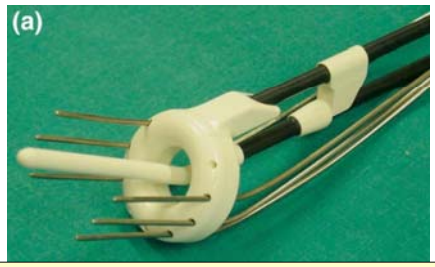
FIGO IIa



FIGO IIIb



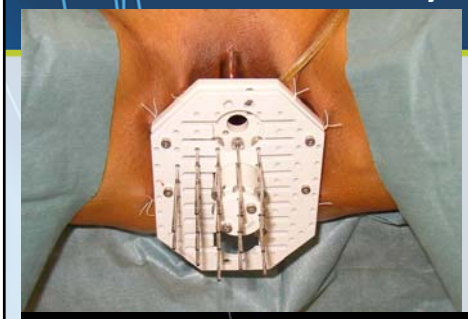
FIGO IVa

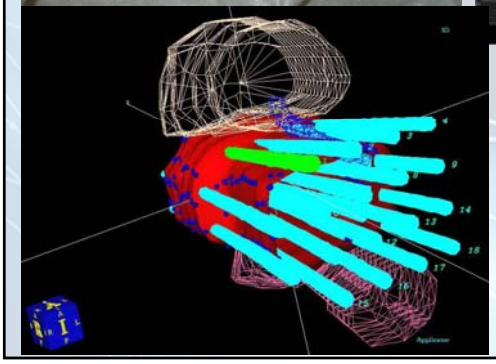


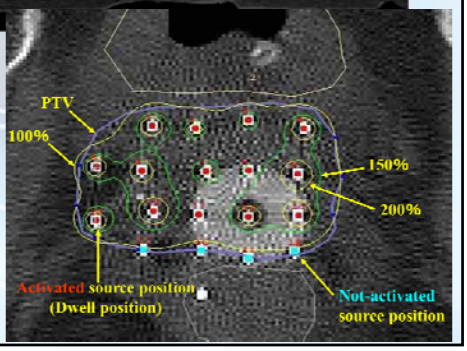
Vienna applicator
(Kirisits, et al. Int J Radiat Oncol Biol Phys 2006;65:624-30)

MUPIT template
(commercially available)

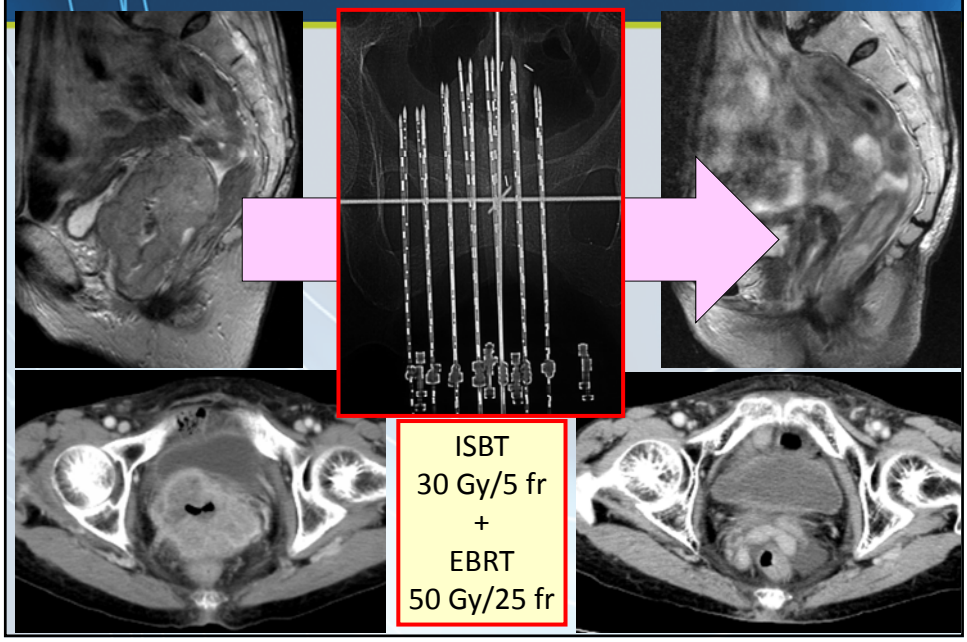
HDR Interstitial Brachytherapy for FIGO IIa Case



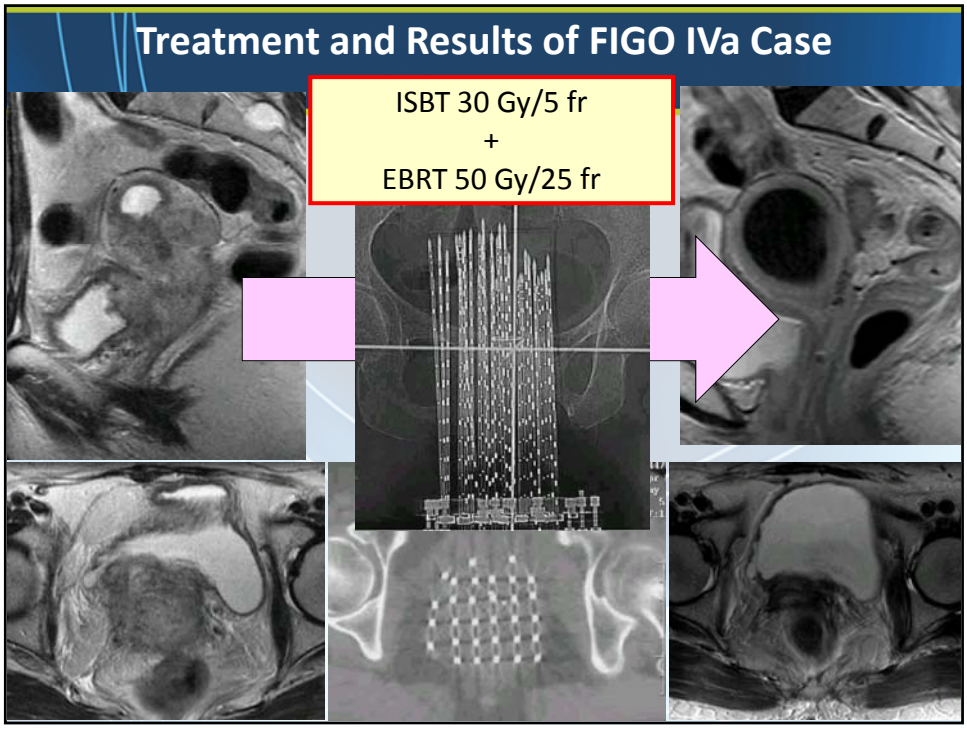




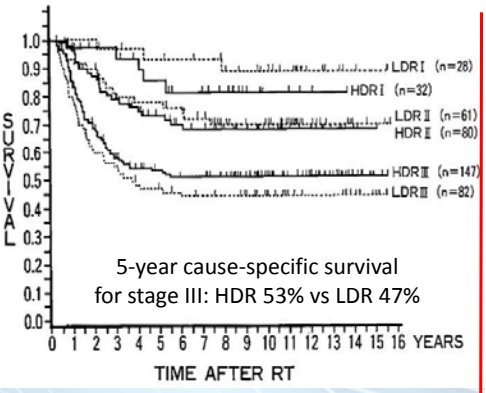
Treatment and Results of FIGO IIIb Case



Treatment and Results of FIGO IVa Case



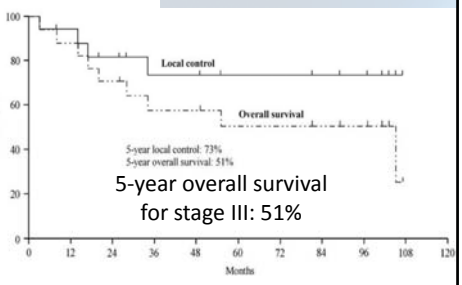
ISBT can maintain satisfactory results even for the patients who would suffer suboptimal brachytherapy with ICBT



5-year cause-specific survival
for stage III: HDR 53% vs LDR 47%

Comparison of LDR vs HDR
in ICBT for Stage I-III cervical cancer

Teshima T, et al. Cancer 72:2409−14,1993



5-year overall survival
for stage III: 51%

HDR－ISBT
for stage III cervical cancer

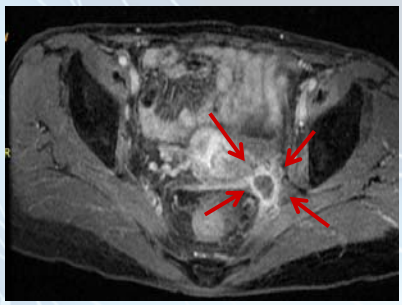
Reason for ISBT (N)
- Too bulky: 20
- Severe invasion to vagina: 5
- Inability to insert tandem: 6

Tumor size: 4-10 cm (median 6 cm)

Isohashi F, et al. Brachytherapy 8:234−9,2009

"HDR Brachytherapy Alone" Salvage RT Policy for In-field Recurrent Cervical Cancer at Osaka University Hospital

Brachytherapy	Dose/fraction/period	N = 54
Intracavitary	30 Gy/5 fr/5 weeks	3
Interstitial	42 Gy/7 fr/4 days	51



Presentation tomorrow Session H2

From 1995, we treat central recurrence of cervical cancer after RT, using high-dose-rate interstitial or intracavitary brachytherapy alone at Osaka University Hospital.
Inoue T, et al. J Brachytherapy Int 1999;15:161-7

Summary of ISBT for Previously Untreated or Previously Treated Cervical Cancer

Previously untreated

Be ambitious to obtain the best dose distribution even for bulky tumor or extremely deviated tumor, using ISBT, otherwise the patients would be poorly treated with ICBT.

Previously treated

Minimize re-irradiated volume to minimize severe toxicity, using ISBT, otherwise the patients have to receive risky surgery or just wait for death.

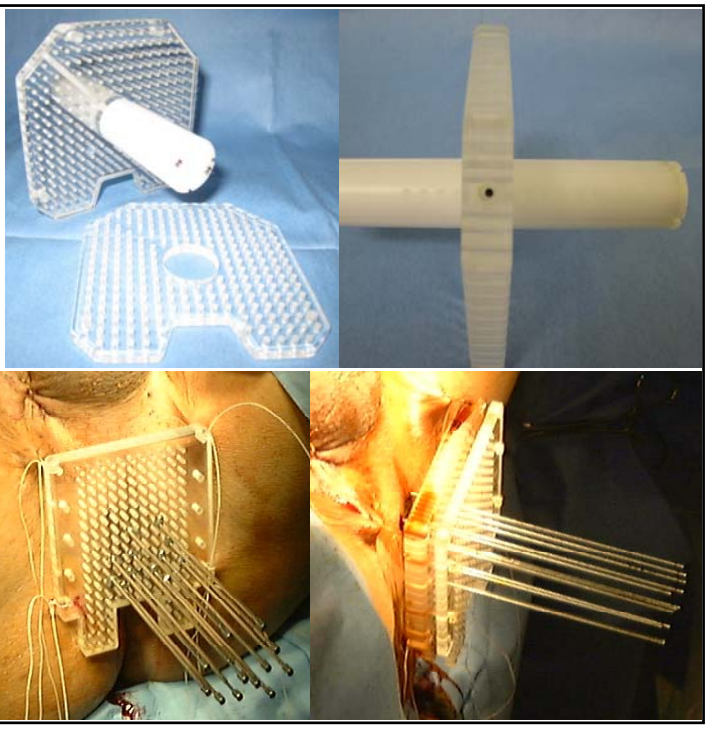
Dr. William Smith Clark
(1826-86)
The first President of Hokkaido University, Japan.
He was also President of The University of Massachusetts Amherst, USA. He is famous for his words:
'Boys, be ambitious.'

In-House Attempt

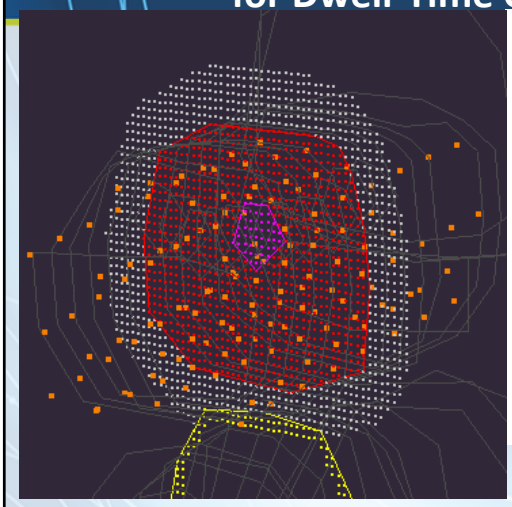
In-house template
(by Yoshioka Y, MD, Osaka Univ.)

In-house optimization software
(by Sumida I, PhD, medical physicist, Osaka Univ.)

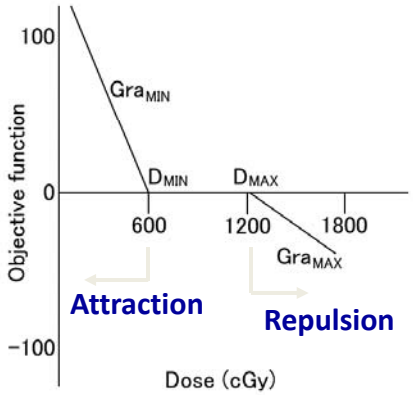
In-house templates for GYN (upper) and Prostate (lower)



Attraction-Repulsion Model for Dwell-Time Optimization

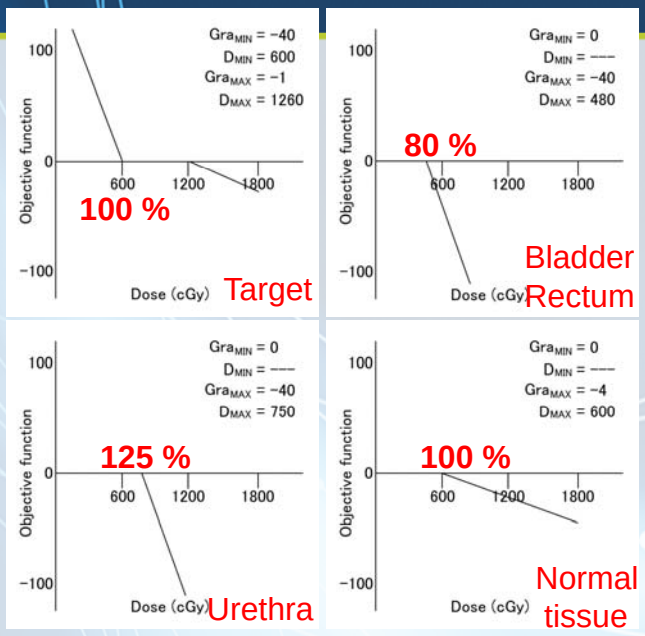


Grid interval: 1 mm
Slice thickness: 3 mm



Gra$_{MIN}$, Gra$_{MAX}$:
The slopes of the linear function.
D$_{MIN}$: The minimum dose
D$_{MAX}$: The maximum dose

Dose Constraints

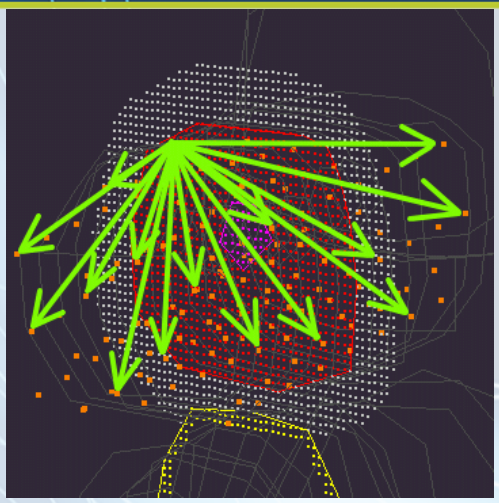


Prescribed dose: 600 cGy

Sumida I, Pouliot J, et al. Int J Radiat Oncol Biol Phys 2006;64:643-649

Calculation Procedure

◎ Set dose constraints



Set initial dwell time (1 sec)

↓

Calculate dose*

↓

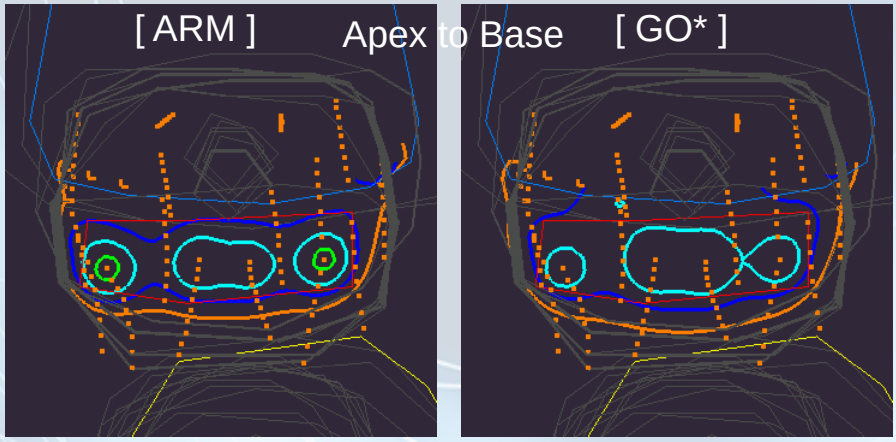
Calculate force

↓

Change dwell time

*: Dose calculation was based on AAPM TG-43.

Comparison of Isodose Distributions

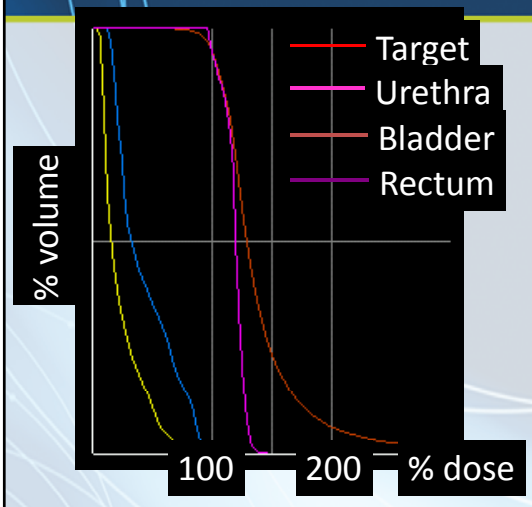


80% 100% 125% 200%

V100 = 95 % of CTV

*: Geometric optimization

Volume Indices



V100	95%
V150	23%
V200	7%
HI*	0.75
COIN*	0.89
V150 Ure	0%

*: Homogeneity index (V100 - V150) / V100
Conformal index (CTVref/CTV) * (CTVref/Vref)

Prostate Brachytherapy Innovations

LDR mono

LDR combi

HDR combi

HDR mono

9 fr → 7 fr → 5 fr
6 fr
4 fr → 2 fr
4 fr → 3 fr
2 fr → 1 fr?

SBRT?

Particle?

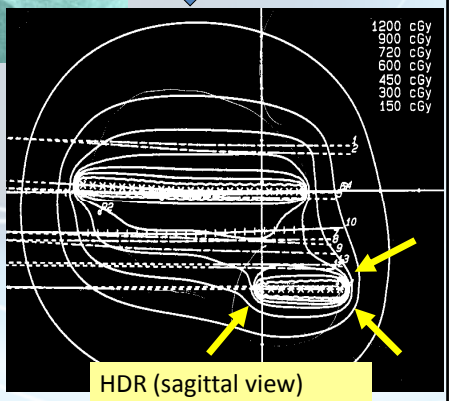
Why HDR?

I-125 seed

If I can adjust any source activity, freely as I like…

If I can place any source outside gland freely as I like…

HDR（planning study）
Urethral dose < prescribed dose (yellow) by inverse planning



HDR (sagittal view)
Arrows: seminal vesicle

Ultimate Form of Boost HDR Concept (Kiel Univ. Germany)

U-shape arrangement of needles

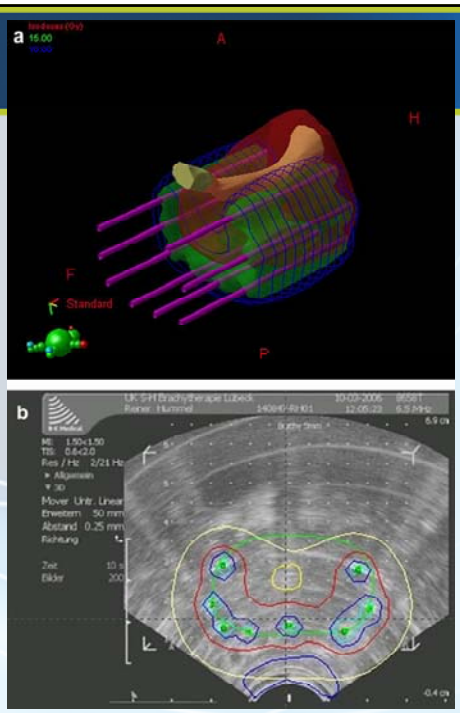
Not cover urethra~anterior portion by prescription dose

↓

Always in combination with EBRT

All in one operation room
(implant→irradiation→removal)
Outpatient treatment

Kovacs. Brachytherapy 6:142-148,2007



How Much Margin Is Needed? Can We Treat it With HDR Monotherapy? → Yes

Table 2. Comparison of postprostatectomy EPE series

Variable	Davis *et al.* (1999)	Sohayda *et al.* (2000)	Teh *et al.* (2003)	Chao *et al.* (2006)	Schwartz *et al.* (2007)
Patients (*n*)	376	265	712	371	404
EPE (%)	105 (28)	92 (35)	299 (42)	121 (33)	121 (30)
Measurable disease	105 (28)	79* (30)	185 (26)	121 (33)	121 (30)
Shrinkage factor	No	No	Yes	Yes	No
PSA of EPE+ patients	11.8 (median) 17.9 (mean)	7.4 (median)	13.73 (mean)	14.5 (mean)	8.5† (median)
Clinical stage (%)					
T1 (%)	163 (T1a-T2a)	36/79 T1c	44 (14.7)	31%	163 (T1a-T2a)
T2 (%)	213 (T2b)	29/79 T2a 9/79 T2b	224 (74.9)	69%	213 (T2b)
T3 (%)	0 (0)	3/79 T3a 2/79 T3b	31 (10.4)	0%	28 (T3)
EPE distance (mm)	0.5 (median) 0.8 (mean)	1.1 (median)	2.0 (median)	2.4 (median) 2.3 (mean)	0.6 (median) 0.9 (mean)
EPE range (mm)	0.04–4.4	0.1–10.0	0.5–12.0	0.05–7.0	0.0–5.7
EPE >5 mm (%)	0 (0)	5 (6)	20 (2.8)	>10%	1 (0.8)
Focal EPE (%)	43 (41)		114 (38.1)		
Extensive EPE (%)	62 (59)		185 (61)		

5-mm margin → enough; 4-mm margin → almost enough
3-mm margin → mostly enough (risk group-dependent?)

Prediction of radial distance of extraprostatic extension from pretherapy factors.
Schwartz DJ, et al. Int J Radiat Oncol Biol Phys 69; 411-8, 2007.

Indication of HDR Monotherapy Is Being Extended to Intermediate-/High-Risk Prostate Cancer

Author [Country]	Total dose/ Fractions	No. of patients	Follow -up (y)	PSA control rate/ Risk group	Late toxicity ≥ Grade 2*	
					GU	GI
Rogers [USA]	39 Gy/6 Fr.	284	2.7	94% (5y)/Intermediate	7.7%	0.0%
Zamboglou [Germany]	38 Gy/4 Fr.	141	4.4	95% (5y)/Low		
	38 Gy/4 Fr.	351		93% (5y)/Intermediate	27.5%	2.6%
	34.5 Gy/3 Fr.	226		93% (5y)/High		
Hoskin [UK]	34 Gy/4 Fr.	34	3.5	95% (3y)/Intermediate	33.0%	13.0%
	36 Gy/4 Fr.	25		87% (3y)/High	40.0%	4.0%
	31.5 Gy/3 Fr.	55			34.0%	7.0%
Yoshioka [Japan]	48 Gy/8 Fr. 54 Gy/9 Fr. 45.5 Gy/7 Fr.	177	6.8	89% (7y)/Intermediate 76% (7y)/High	12.4%	4.5%

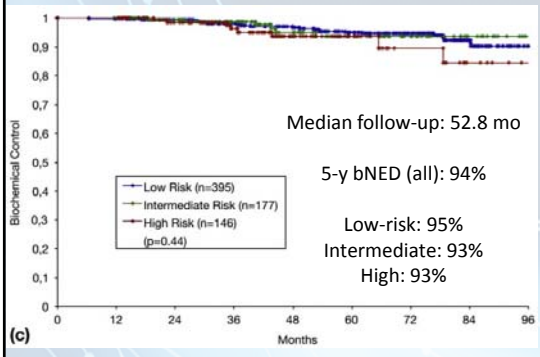
*Scored per event not per patient.

Rogers CL, et al. J Urol 2012;187:109-16
Zamboglou N, et al. Int J Radiat Oncol Biol Phys 2013;85:672-8
Hoskin P, et al. Int J Radiat Oncol Biol Phys 2012;82:1376-84
Yoshioka Y, et al. ESTRO 33, 2014

Largest Series of HDR Monotherapy for Low-, Intermediate-, and High-Risk Prostate Cancer

718 patients (low-high risk) treated by HDR monotherapy

9.5 Gy x 4 fr (1 implant) (2 days) → 9.5 Gy x 4 fr (2 implants) (2 weeks) → 11.5 Gy x 3 fr (3 implants) (3 weeks)



Median follow-up: 52.8 mo

5-y bNED (all): 94%

Low-risk: 95%
Intermediate: 93%
High: 93%

Hormone therapy (median mo (range))

Low: 4 (3-6)
Inter: 6 (6-10)
High: 9 (9-14)

Overall: 9 (3-14)

Toxicity (per event)

Acute GU G3: 5.4%
Acute GI G3: 0.2%
Late GU G3: 3.5%
Late GI G3: 1.6%
(None G4-5)

Zamboglou N, et al. Int J Radiat Oncol Biol Phys 2013;85:672-8 (Offenbach, Germany)

Clinical Investigation: Genitourinary Cancer

High-Dose-Rate Brachytherapy as Monotherapy Delivered in Two Fractions Within One Day for Favorable/Intermediate-Risk Prostate Cancer: Preliminary Toxicity Data

Michel Ghilezan, M.D., Ph.D., Alvaro Martinez, M.D., Gary Gustason, M.D., Daniel Krauss, M.D., J. Vito Antonucci, M.D., Peter Chen, M.D., James Fontanesi, M.D., Michelle Wallace, R.N., Hong Ye, M.S., Alyse Casey, R.N., Evelyn Sebastian, B.S., Leonard Kim, M.S., and Amy Limbacher, B.S.

Department of Radiation Oncology, William Beaumont Hospital and Rose Cancer Institute, Royal Oak, Michigan

13.5 Gy x 2 fr (one day)
William Beaumont
Ghilezan et al.
Int J Radiat Oncol Biol Phys 2012;83:927-32

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journal homepage: www.thegreenjournal.com

ELSEVIER

Prostate brachytherapy

High-dose-rate brachytherapy alone given as two or one fraction to patients for locally advanced prostate cancer: Acute toxicity

Peter Hoskin, Ana Rojas*, Peter Ostler, Robert Hughes, Roberto Alonzi, Gerry Lowe, Linda Bryant

Cancer Centre, Mount Vernon Hospital, Middlesex, UK

13 Gy x 2 fr, 19 Gy x 1 fr, 20 Gy x 1 fr
Mount Vernon (UK), Hoskin et al. Radiother Oncol 2014;110:268-71

Where Are HDR and SBRT Standing?

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2014
Prostate Cancer

NCCN Guidelines Index
Prostate Table of Contents
Discussion

PRINCIPLES OF RADIATION THERAPY

Presentation tomorrow Session F2 (SBRT vs HDR)

Primary External Beam Radiation Therapy (EBRT)

- Highly conformal RT techniques should be used to treat prostate cancer.
- Doses of 75.6 to 79.2 Gy in conventional fractions to the prostate (± seminal vesicles for part of the therapy low-risk cancers. For patients with intermediate- or high-risk disease, doses up to 81.0 Gy provide improve
- Moderately hypofractionated image-guided IMRT regimens (2.4 to 4 Gy per fraction over 4-6 weeks) have be reporting similar efficacy and toxicity to conventionally fractionated IMRT. They can be considered as an al fractionated regimens when clinically indicated.
- Extremely hypofractionated image-guided IMRT/SBRT regimens (6.5 Gy per fraction or greater) are an emerging treatment modality with single institutional and pooled reports of similar efficacy and toxicity to conventionally fractionated regimens. They can be considered as a cautious alternative to conventionally fractionated regimens at clinics with appropriate technology, physics, and clinical expertise.
- Patients with high-risk cancers are candidates for pelvic lymph node irradiation and the addition of neoadjuvant/concomitant/adjuvant ADT for a total of 2 to 3 y (category 1).
- Patients with intermediate-risk cancer may be considered for pelvic lymph node irradiation and 4- to 6-mo neoadjuvant/concomitant/adjuvant ADT.
- Patients with low-risk cancer should not receive pelvic lymph node irradiation or ADT.
- The accuracy of treatment should be improved by attention to daily prostate localization, with techniques of IGRT using CT, ultrasound, implanted fiducials, electromagnetic targeting/tracking, or an endorectal balloon to improve oncologic cure rates and reduce side effects.

Primary/Salvage Brachytherapy

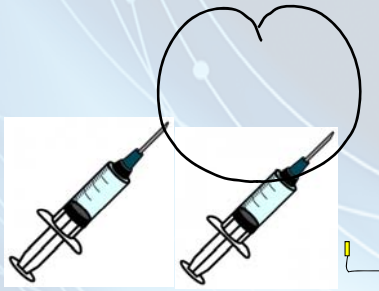
- Permanent low-dose rate (LDR) brachytherapy as monotherapy is indicated for patients with low-risk cancers. For intermediate-risk cancers, consider combining brachytherapy with EBRT (40-50 Gy) ± 4- to 6-mo neoadjuvant/concomitant/adjuvant ADT. Patients with high-risk cancers may be treated with a combination of EBRT (40-50 Gy) and brachytherapy ± 2 to3 y-neoadjuvant/concomitant/adjuvant ADT.
- Patients with a very large prostate or very small prostate, symptoms of bladder outlet obstruction (high IPSS), or a previous transurethral resection of the prostate are more difficult to implant and may suffer increased risk of side effects. Neoadjuvant ADT may be used to shrink the prostate to an acceptable size; however, increased toxicity would be expected from ADT and prostate size may not decline.
- Post-implant dosimetry must be performed to document the quality of the implant.
- The recommended prescribed doses for LDR monotherapy are 145 Gy for Iodine-125 and 125 Gy for Palladium-103. The corresponding boost doses after 40 to 50 Gy EBRT are 110 Gy and 90 to 100 Gy, respectively.
- High-dose rate (HDR) brachytherapy can be used alone or in combination with EBRT (40-50 Gy) instead of LDR. Commonly used boost regimens include 9.5 to 11.5 Gy x 2 fractions, 5.5 to 7.5 Gy x 3 fractions, and 4.0 to 6.0 Gy x 4 fractions. A commonly used regimen for HDR treatment alone includes 13.5 Gy x 2 fractions.
- Permanent LDR or temporary HDR brachytherapy can be used as treatment for a local recurrence following EBRT or primary brachytherapy. Radiation dose depends on the original primary external beam dose and ranges from 100 to 110 Gy for LDR and 9 to 12 Gy x 2 fractions for HDR.

Representative Dose-Fractionations and BEDs of SBRT or HDR

		Physical dose			BED (Gy)		EQD_{2Gy} (Gy)	
Method	Author	Dose/fr (Gy)	No. of fractions	Total dose (Gy)	α/β =1.5	α/β =3.0	α/β =1.5	α/β =3.0
SBRT	McBride (Multicenter, prospective)	7.25	5	36.25	211	124	91	74
		7.5	5	37.5	225	131	96	79
SBRT	Katz	7	5	35	198	117	85	70
		7.25	5	36.25	211	124	91	74
SBRT	King (Multicenter, pooled)	7-8, Median 7.25	5	35-40, Median 36.25	198	117	85	70
					253	147	109	88
HDR	Yoshioka	6	9	54	270	162	116	97
HDR	Yoshioka	6	8	48	240	144	103	86
HDR	Yoshioka	6.5	7	45.5	243	144	104	86
HDR	Rogers	6.5	6	39	208	124	89	74
HDR	Demanes	7	6	42	238	140	102	84
HDR	Mark	7.5	6	45	270	158	116	95
HDR	Martinez	9.5	4	38	279	158	119	95
HDR	Zamboglou	11.5	3	34.5	299	167	128	100
HDR	Hoskin	13	2	26	251	139	108	83
HDR	Ghilezan	13.5	2	27	270	149	116	89
HDR	Hoskin	19	1	19	260	139	111	84
IMRT	Zelefsky	1.8	48	86.4	190	138	81	83

What's Next ?

Minimum HDR source
Outpatient-based clinic
(eg: 12 Gy x 3 fr, weekly)



You feel something pricking.
See you next week!

Radio-controlled
self-propelling source

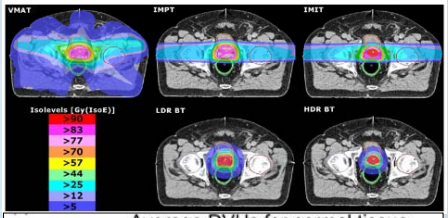
You do practice in driving a
radio-controlled model car!

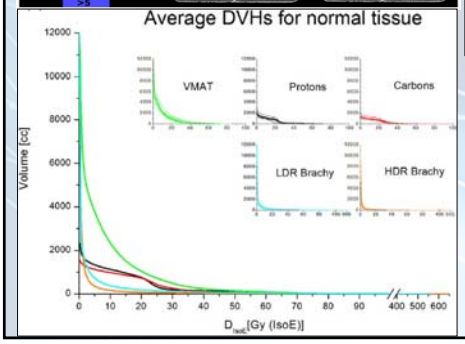
What's "the Best Radiotherapy"?

Physics Contribution

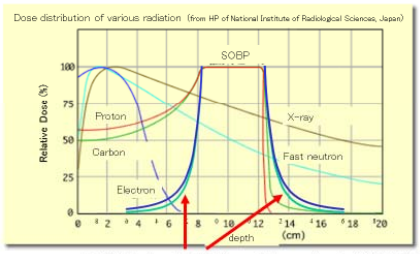
Georg D, et al. Int J Radiat Oncol Biol Phys 88;715-22,2014

Dosimetric Considerations to Determine the Optimal Technique for Localized Prostate Cancer Among External Photon, Proton, or Carbon-Ion Therapy and High-Dose-Rate or Low-Dose-Rate Brachytherapy





Can not SOBP be mimicked by brachytherapy??
(moreover, also at beam inlet?!)



Ir-192 (blue) and I-125 (green): According to AAPM TG-43, considering the inverse square law and the radial dose function

"Inverse square law"
is the strongest tool
among all radiotherapy,
And it provides ample room for
YOU to develop
a new treatment application.