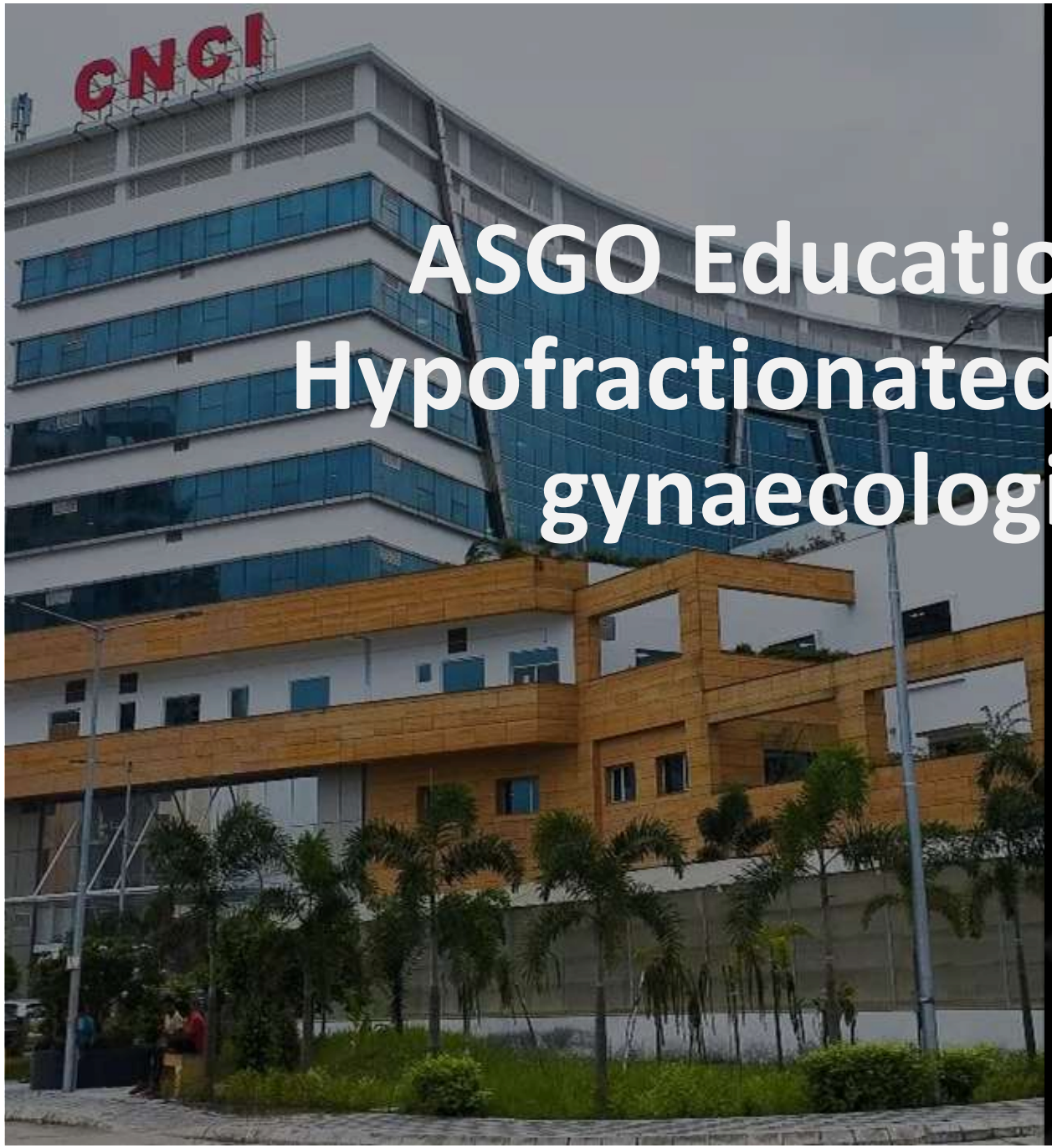

ASGO Education- Discussion: Hypofractionated Radiotherapy in gynaecological cancers

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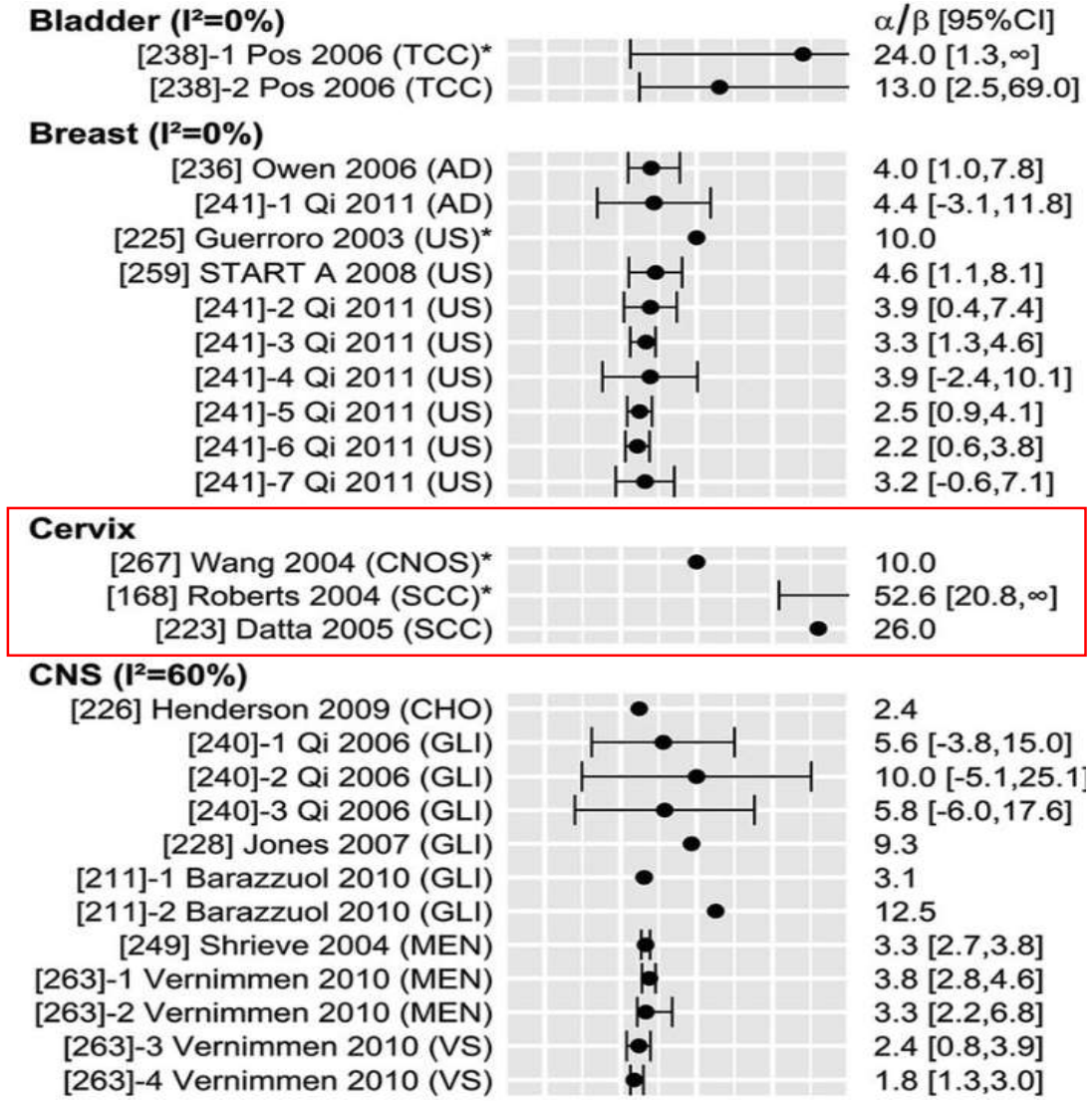
Radiobiological rationale of hypofractionation in gynaecological malignancies: α/β, OTT, Histology…

The alfa and beta of tumours: a review of parameters of the linear-quadratic model, derived from clinical radiotherapy studies



α/β depend on:

- Tumor site
- Tumor histology

van Leeuwen et al. Radiation Oncology (2018) 13: 96-106

Overall treatment time in advanced cervical carcinomas: A critical parameter in treatment outcome

- 386 patients of stage IIB and III carcinoma cervix
- Highly significant factors for reduced local control and OS:
- Blood transfusion
- Overall treatment time
- OTT > 52 days: LC and OS reduce by 1% per day

Girinsky T, et al. Int J Rad Oncol Biol Phy 1993; 27(5): 1051-1056

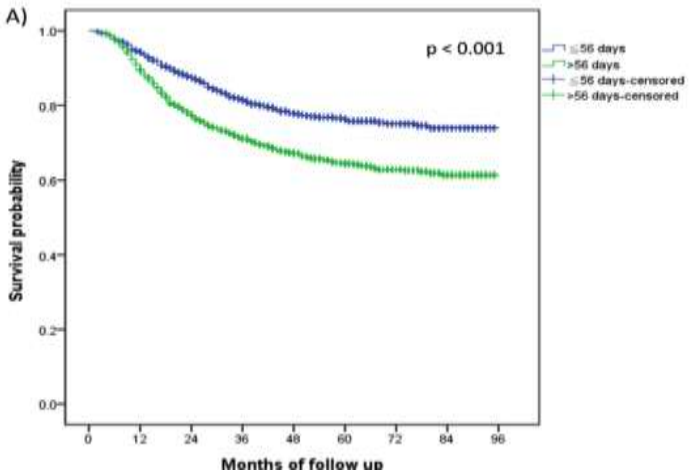
The prognostic impact of overall treatment time on disease outcome in uterine cervical cancer patients treated primarily with concomitant chemoradiotherapy: a nationwide Taiwanese cohort study

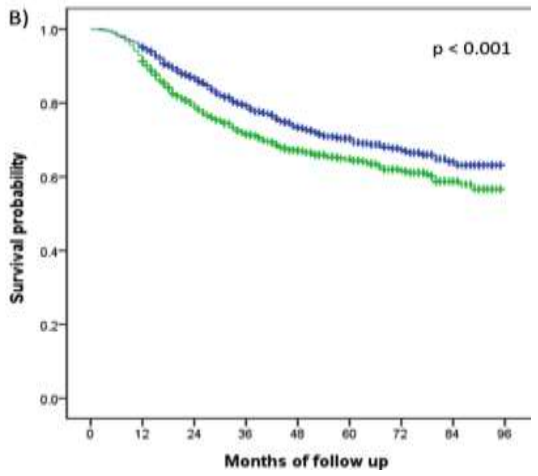
- Population based cohort study
- 2594 patients of stage I-IVA cervical cancer
- Median irradiation duration: 59 days
- Significant prognostic factors related to poor CSS and OS:

- Old age
- Non-squamous cell cancer type
- Increased tumor size
- High grade
- Increased OTT
- Advanced stage

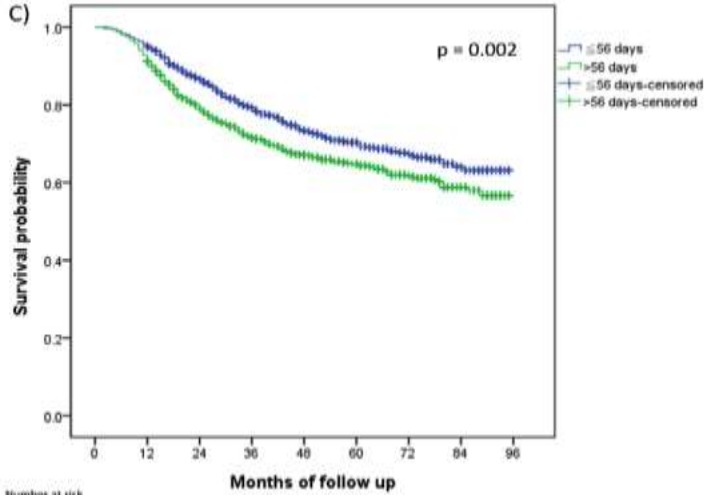
Lin SM, et al. Oncotarget 2017; 8(49): 85203-85213

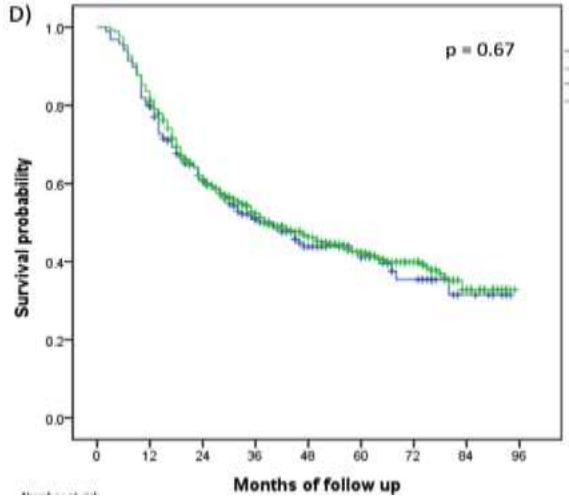
The prognostic impact of overall treatment time on disease outcome in uterine cervical cancer patients treated primarily with concomitant chemoradiotherapy: a nationwide Taiwanese cohort study



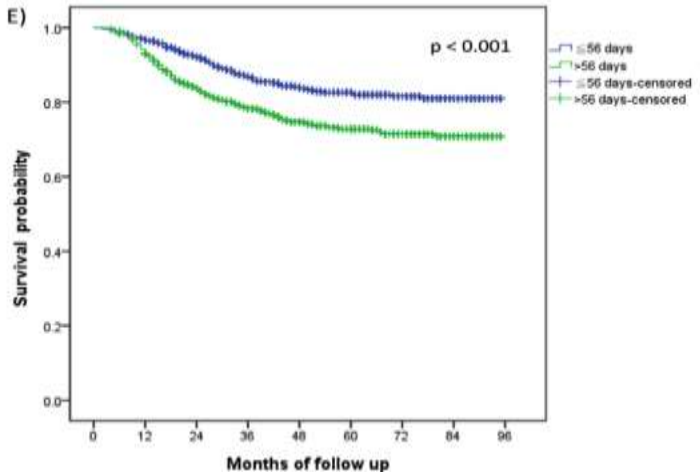


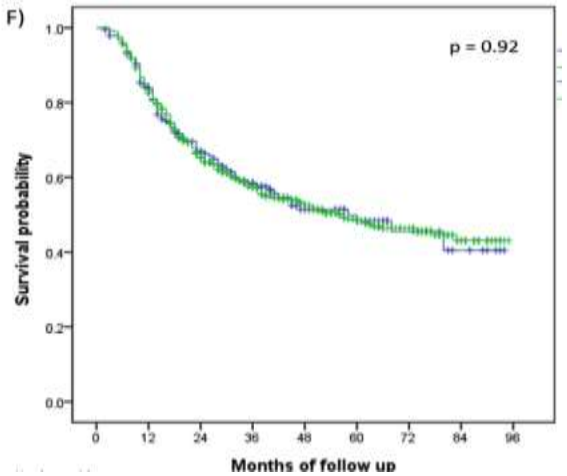
CSS & OS for all patients





OS for I-IIB & III-IVA





CSS for I-IIB & III-IVA

Completion of CCRT recommended particularly for stage I-IIB patients

Lin SM, et al. Oncotarget 2017; 8(49): 85203-85213

SBRT boost after EBRT…

Ongoing Trials…

Author (setting)	n	Stage	Patients' inclusion	Median follow-up (range)	EBRT	SBRT boost technique & dose	Treatment outcome		Grade ≥ 3 toxicity
							OS	LC	
Haas et al. [47] (R)	6	IIB (4), IV (2)	Not suitable for BT or refuse BT	14 mo (1–28)	45 Gy/25 fx	CK & 20 Gy/5 fx or 19.5 Gy/3 fx	100%	100% in 5 pts with a minimum of 1 year	None
Marnitz et al. [48] (R)	11	IIB (9), IIIB (2)	Not suitable for BT	6 mo	50.4 Gy/28 fx	CK & 30 Gy/5 fx	100%	100%	None
Ito et al. [49] (P, Phase I)	6	IIIA (2), IIIC (4)	Not suitable for BT	17 mo (8–32)	45 Gy/25 fx	LINAC & 19.5–22.5 Gy/3 fx	NA	100%	None
Facondo et al. [50] (R)	9	II (5), III (2), IVA (2)	Not suitable for BT	16 mo (6–58)	50.4 Gy/28 fx	LINAC & 12–25 Gy/2–5 fx	2-year 70%	1 recurrence	Acute: None
Hsieh et al. [51] (R)	9	IIB (4), IIIB (3), IVA (2)	Not suitable for BT	36 mo	50–50.4 Gy/25–28 fx	Tomotherapy & 16–27 Gy/5–9 fx	47%	78%	Acute: 2 pts
Morgenthaler et al. [52] (R)	31	I (2), II (20), III (4), IVA (5)	Not suitable for BT or refuse BT	40 mo (5–84)	50.4 Gy/28 fx	CK & 25–30 Gy/5 fx	3-year 60%	3-year 92%	Acute: 1 pt
Lee et al. [54] (R)	25	I-II (11), III (9), IV (5)	Not suitable for BT	34 mo (4–79)	44–50.4 Gy/25–28 fx	LINAC & 20–33 Gy/4–6 fx	3-year 41%	3-year 81%	5/21 pts (23.8%)
Albuquerque et al. [53] (P, Phase II)	12	I-II (7), III (6), IV (2)	Not suitable for BT or refuse BT	19 mo	45 Gy/25 fx	LINAC & 28 Gy/4 fx	2-year 53%	2-year 70%	2-year 26.7%

Understanding…

- Impressive LC and OS data with EBRT and HDR-ICBT (MRI based)

- Use of brachytherapy decreasing due to
- Shortage of human manpower
- High expenses for source replacement
- Low medical reimbursement

- Lack of prospective RCTs

- 3 studies reported OS & LC of 100% with no >Grade 3 adverse effects (6 & 11 patients & <2 yrs followup)

- Difficult to recommend specific dose regimen for SBRT (varies between 23.4- 40Gy)

- May be more effective in higher stage tumors

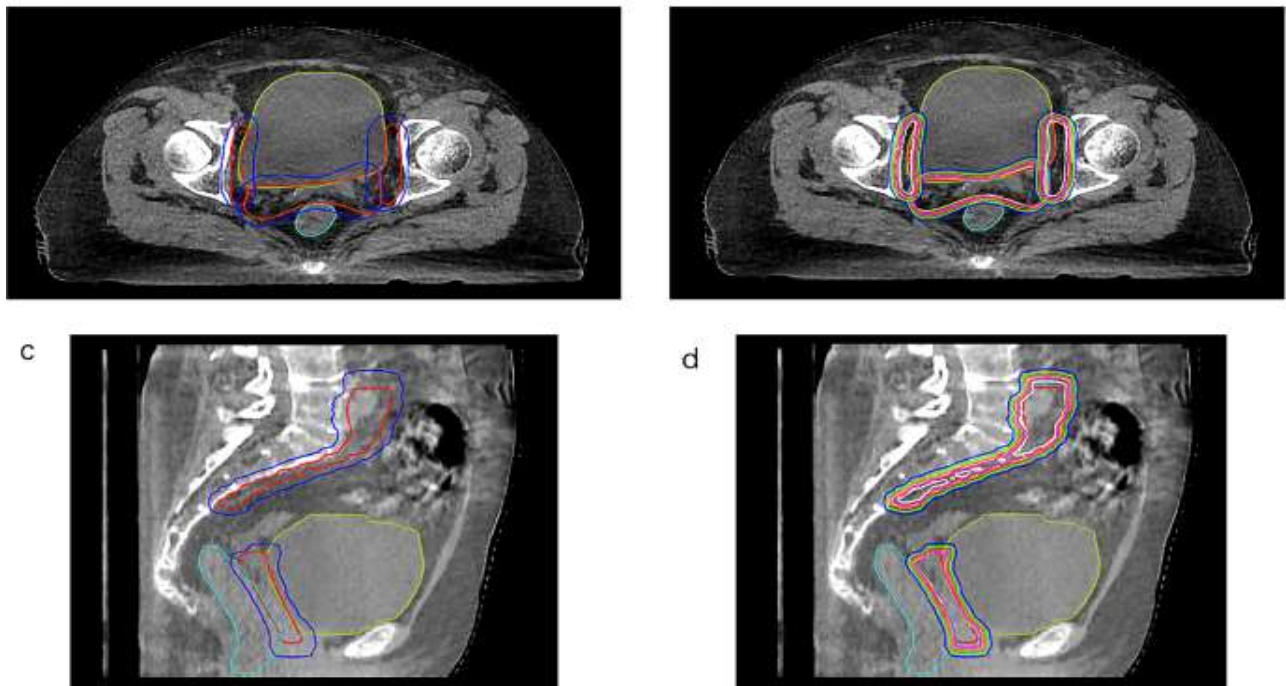
How will you be extra cautious while treating postoperative patients with hypofractionated radiotherapy?

Trials of hypofractionated post op RT…

Author (setting)	n	Primary	Combined treatments	Median follow-up	Radiation technique & dose	Treatment outcome		Toxicity
						OS	LC	
Leung et al. [55] (P, Phase I/II)	61	EM	Sequential CTx (16), vaginal BT (9)	9 mo (IQR, 3–15)	VMAT & 30 Gy/5 fx (EOD or weekly)	NA	NA	GI: G2 (13%), G3 (1.6%) GU: G2 (3%)
Koukourakis et al. [56] (R)	25	EM (22), Cx (3)	Cytoprotetion (amifostine)	31 mo	3D-CRT & 37.8 Gy/14 fx followed by boost 12 Gy/3–4 fx	100%	100%	Acute: G2 (8%) Late: G2 (4%) No G3
Kim et al. [57] (C)	1	Cx	None	1 mo	IMRT & 40 Gy/16 fx	NA	NA	Sigmoid perforation at 1 mo

Precautionary measures…

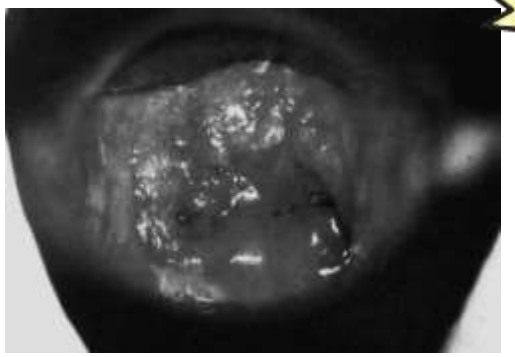
- Use of advanced technology (IMRT, IGRT…)
- Strict bladder filling
- How to ensure rectal volume?
- Use of prone technique?
- Role of Amifostine?

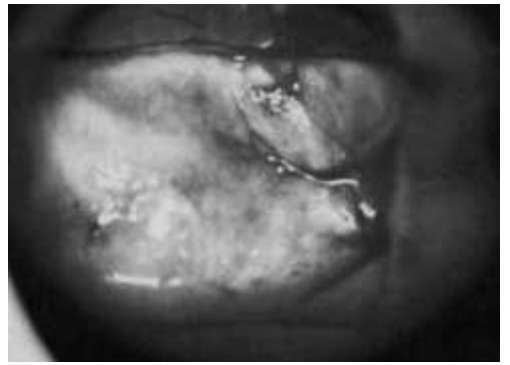


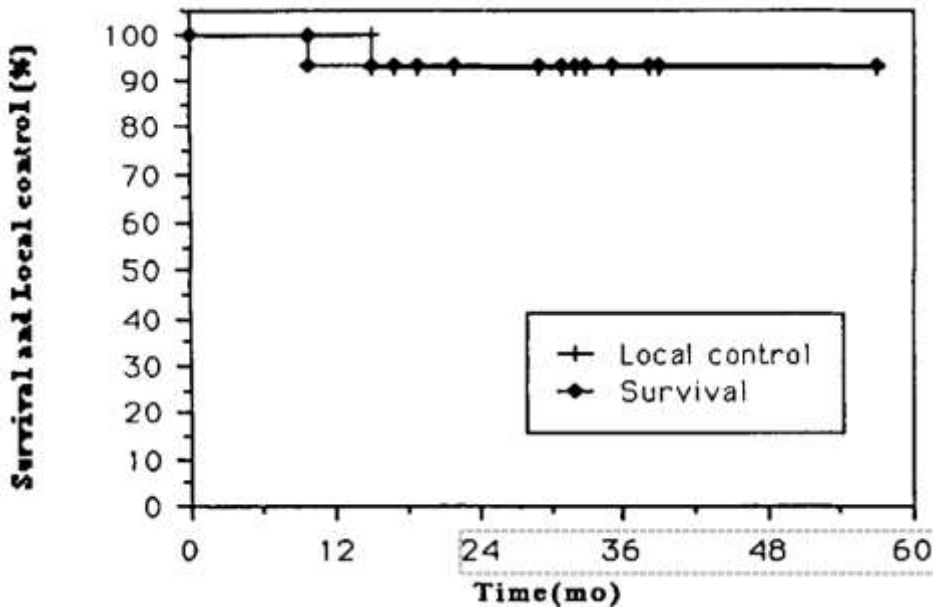
Can particle beam hypofractionated radiotherapy replace brachytherapy?

High-Energy Proton Beam Radiation Therapy for Gynecologic Malignancies
Potential of Proton Beam as an Alternative to Brachytherapy

Patient no.	Age (yr)	Sex	Tumor site	FIGO	Volume*	Dose(x)†	Dose(p)‡	Comment
1	70	F	Cervix	IIB	273	32.4/18	38.5/13	NED 57 mo
2	69	F	Cervix	IIB	139	0	82.0/25	NED 38 mo
3	67	F	Cervix	IIIB	132	0	74.5/17	Recurrence
4	58	F	Cervix	IIB	169	0	75.0/17	NED 39 mo
5	61	F	Cervix	IIB	195	30.6/17	48.5/19	NED 33 mo
6	67	F	Cervix	IIIB	255	30.6/17	61.2/21	NED 32 mo
7	70	F	Cervix	IIIB	245	25.2/14	58.0/18	NED 31 mo
8	67	F	Cervix	IIIB	170	25.2/14	61.0/18	NED 29 mo
9	65	F	Cervix	IIB	250	0	84.0/28	NED 22 mo
10	49	F	Cervix	IIIB	595	28.8/16	76.0/20	Dead PA LN
11	73	F	Cervix	IIB	259	0	86.5/25	NED 17 mo
12	60	F	Cervix	IIIB	315	14.4/8	85.2/24	NED 17 mo
13	58	F	Corpus	III	441	37.8/21	101.3/25	NED 15 mo
14	64	F	Vagina	II	135	30.6/17	37.5/17	NED 35 mo
15	68	F	Vagina	II	162	0	90.0/28	NED 19 mo







- Target dose: >80Gy in most patients
- 2 yr local control rate: 92.3%
- 2 yr survival rate: 93.3%
- Only one patient had local recurrence (14/15 patients were LR controlled at 15-57 months)
- 2 patients had Grade II radiation proctitis only
- Sharply localized PBT produce antitumor effect equivalent to conventional brachytherapy

Arimoto T, et al. Cancer 1991; 68: 79-83

LONG-TERM RESULTS OF PROTON BEAM THERAPY FOR CARCINOMA OF THE UTERINE CERVIX

- 25 patients of carcinoma cervix treated with. 50.4Gy/28# of photon RT to whole pelvis with central shielding placed after 25Gy followed proton RT to primary tumor and adjacent tissue to a dose of 61Gy @ 2.5-4 Gy/#
- OS at 10 yrs: 59% (for stage IIB-89% and for stage IIIB/IVA- 40%)
- Cause specific survival at 10 yrs: 65%
- 5-yr local control rate for stage IIB: 100% and for all patients was 75%

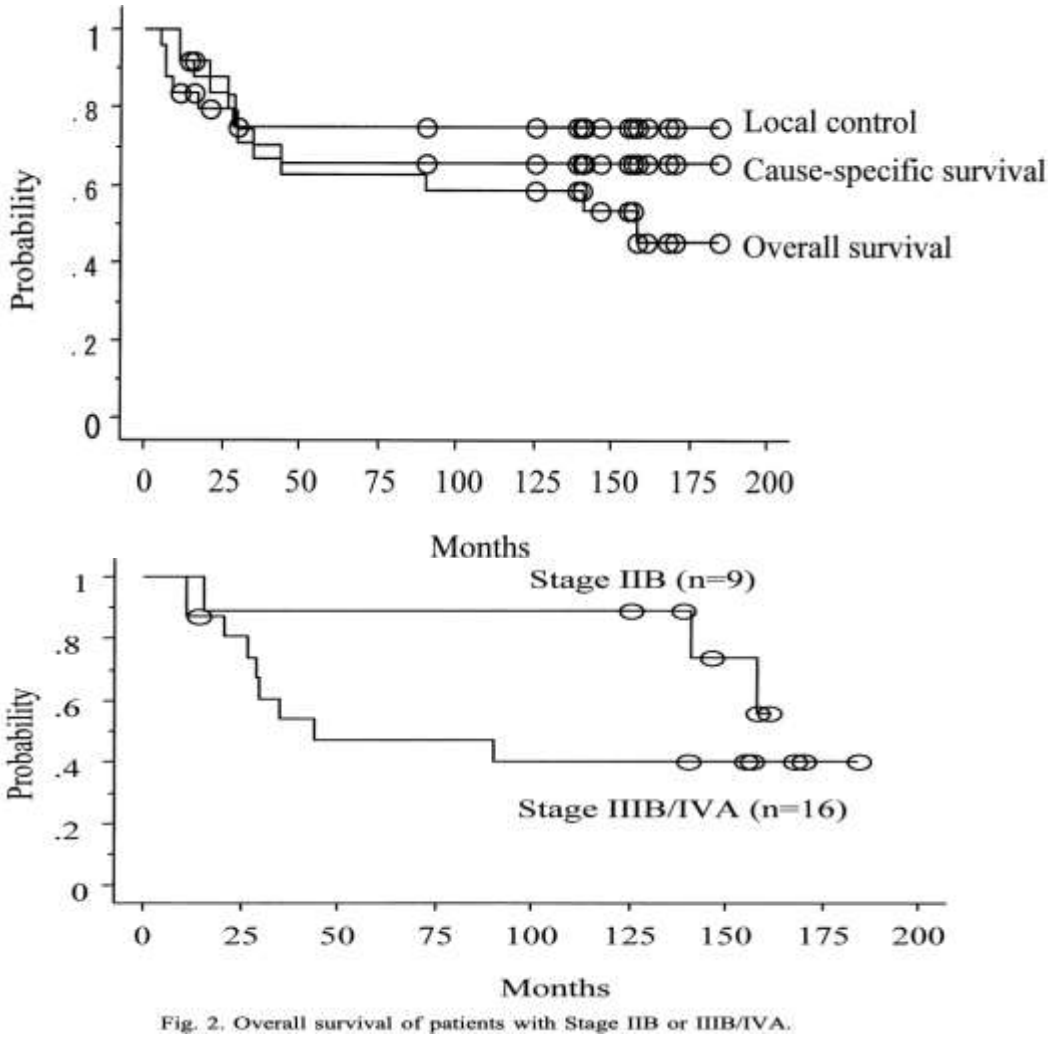


Fig. 2. Overall survival of patients with Stage IIB or IIIB/IVA.

Kagei K, et al. Int. J. Radiation Oncology Biol. Phys. 2003; 55(5): 1265–1271


thank you
danke
謝謝
ngiyabonga
teşekkur ederim
спасибо
gracias
dank je
dziękuje
bedankt
obrigado
sukriya
kop khun krap
go raibh maith agat
grazie
arigato
dakujem
merci
мерси