


How can radiation therapy support the global strategy to eliminate cervical cancer?



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Epidemiology



4th rank of all cancers
2nd rank for 11-44 years

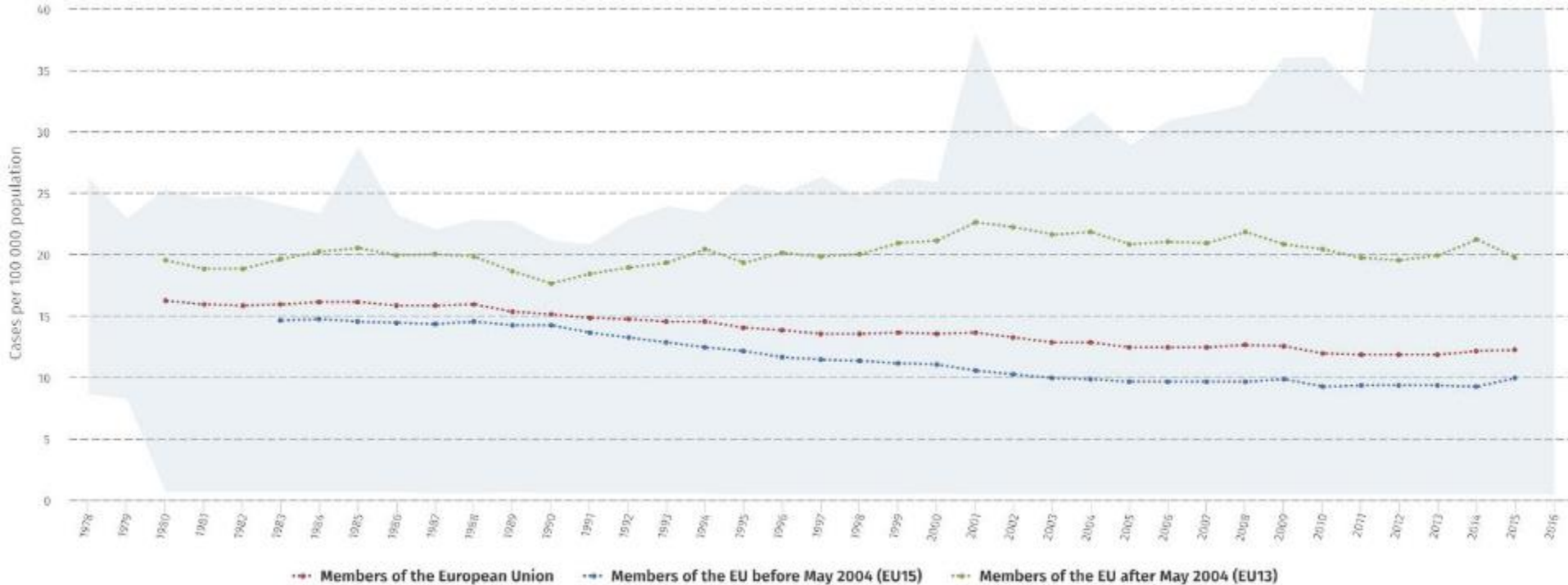


Worldwide, 2018
570 000 cases
More than 310 000 deaths

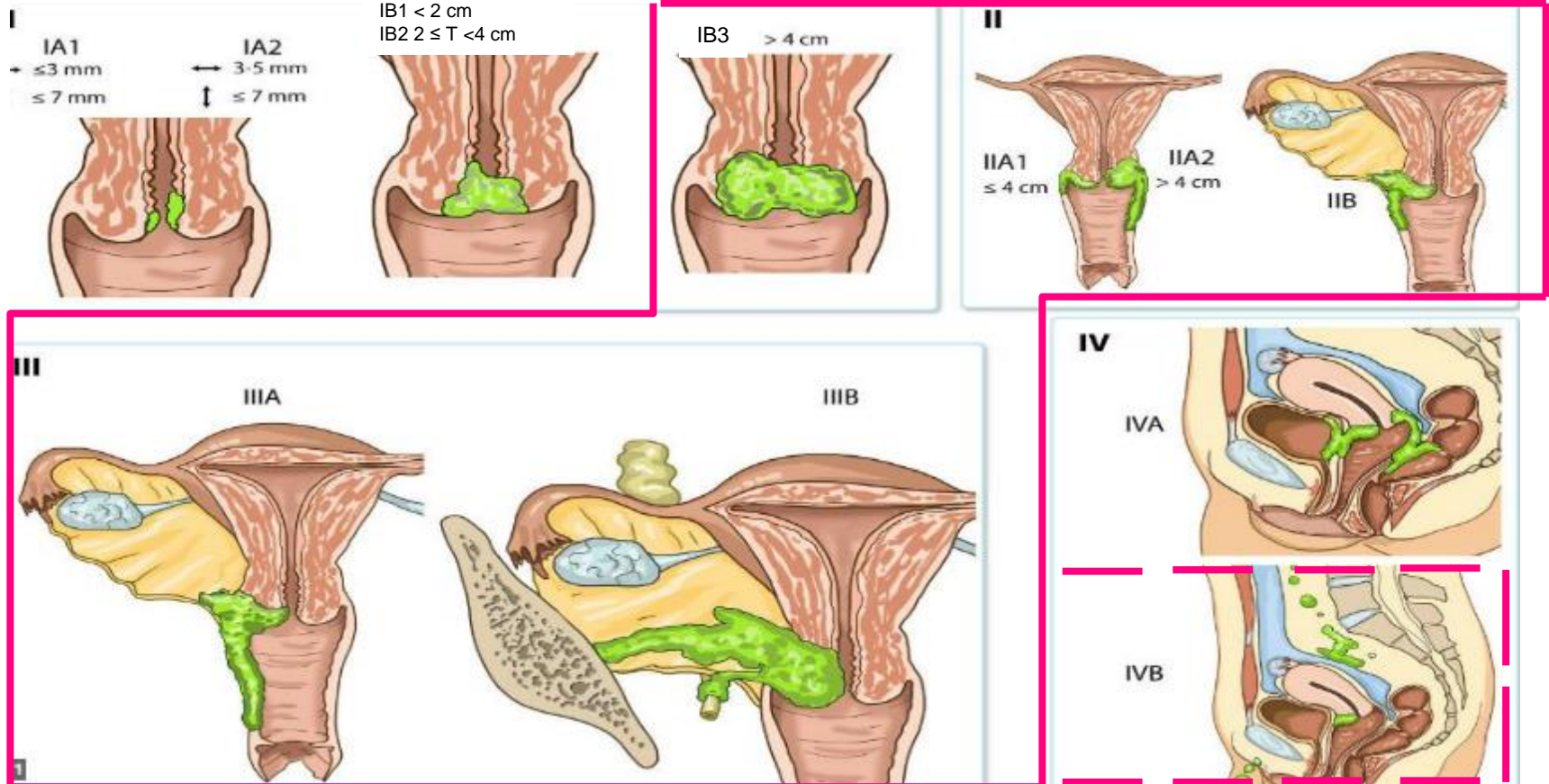
Arbyn M, Weiderpass E, Bruni L, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. Lancet Glob. Health. 2020
Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA. Cancer J. Clin. 2020

WHO European Health Information Gateway

Incidence of cervix uteri cancer per 100 000



Classification FIGO 2018



Radiation therapy

Table 1. Carcinoma of the uterine cervix: Disease-free survival and incidence of tumor recurrence

Stage	No. of patients	10-year disease-free survival rate	Site of recurrence			
			Pelvic only	Pelvic and distant metastases	Total pelvic failures	Distant metastases only
IA	43	98%	0	1 (2)	1 (2)	1 (2)
IB	493	82%	18 (4)	40 (8)	58 (12)	50 (10)
IIA	151	65%	7 (5)	23 (15)	30 (20)	27 (18)
IIB	433	65%	45 (10)	47 (11)	92 (21)	69 (16)
III	350	40%	59 (17)	84 (24)	143 (41)	72 (21)
IVA	29	4%	11 (38)	10 (34)	21 (72)	6 (21)

Data are *n* (%).

TABLE 1. ESTIMATES OF THE RELATIVE RISK OF DEATH IN FIVE CLINICAL TRIALS OF CONCURRENT CHEMOTHERAPY AND RADIO THERAPY.

STUDY	FIGO STAGE*	TREATMENT		RELATIVE RISK OF DEATH IN COMPARISON GROUP
		CONTROL GROUP	COMPARISON GROUP	
Keys et al. ¹	IB2	Radiotherapy	Radiotherapy plus weekly cisplatin	0.54
Rose et al. ²	IIB–IVA	Radiotherapy plus hydroxyurea	Radiotherapy plus weekly cisplatin Radiotherapy plus cisplatin, fluorouracil, and hydroxyurea	0.61 0.58
Morris et al. ³	IB2–IVA	Extended-field radiotherapy	Radiotherapy plus cisplatin and fluorouracil	0.52
Whitney et al. ⁵	IIB–IVA	Radiotherapy plus hydroxyurea	Radiotherapy plus cisplatin and fluorouracil	0.72
Peters et al. ⁶	IB or IIA (selected postoperatively)	Radiotherapy	Radiotherapy plus cisplatin and fluorouracil	0.5

*FIGO denotes the International Federation of Gynecology and Obstetrics.

Toxicities

Table 3
Acute toxicity grades for each trial specified in standard versus chemoradiation status

	Chemoradiation				Radiotherapy			
	1 and 2		3 and 4		1 and 2		3 and 4	
	Number	%	Number	%	Number	%	Number	%
Haemoglobin [21,28,32,42,44,45]	448/1141	39.3	78/1201	6.5	231/796	29.0	35/858	4.1
WCC [15,21,28,31,32,42,44,45]	656/1328	49.4	227/1388	16.4	393/982	40	82/1044	7.9
Platelets [15,21,28,31,32,42,44,45]	251/1223	20.5	22/1283	1.7	87/874	10	4/936	0.4
Haematology* NOS [17,20,23]	104/195	53.3	112/378	27.6	34/198	17.2	5/379	1.3
Genitourinary [17,23,28,32,42]	198/1133	17.5	21/1358	1.5	165/966	17.1	19/1191	1.6
Gastrointestinal [17,23,28,32,42]	530/1172	45.2	112/1397	8	404/991	40.8	51/1216	4.2
Neurological [23,28,32,42]	52/836	6.2	5/836	0.6	18/670	2.7	3/670	0.5
Skin [17,23,28,32,42]	161/1028	15.7	23/1223	1.9	113/858	13.2	13/1051	1.2

Combined grades of toxicity at each ranking, 1 and 2, 3 and 4 added together, with combined denominator shown with grading as adopted by individual authors. References for included trials are shown in parentheses.

Table 4
Chemoradiation in cervical cancer: comparison of long-term toxicity across trials specified

Trial	Chronic toxicity	Genitourinary	Gastrointestinal	Neurological	Fistula	Other	Overall	Comments	Follow-up		
									Minimum	Maximum	Median
Keys [17]	Yes	–	–	–	–	–	No diff	Same number of fistula and bowel	11 ^a	61 ^a	36
Morris [23]	Yes	Bladder/ureters	Small/large bowel and rectum	–	–	34	No diff	–	0 ^a	86	43 ^a
Peters [28]	Yes	1234	1234	–	–	–	–	–	12 ^a	72 ^a	42
Pras	No	–	–	–	–	–	–	–	–	–	–
Rose [32]	No	–	–	–	–	–	–	–	5 ^a	65 ^a	35
Tseng [39]	Yes	Radical cystitis	Radical proctitis	3 + 4	3 + 4	Intestinal obstruction	3 + 4	CRT 23.3% RT 12.9%	12	69	46.8
Whitney [42]	Yes	–	–	–	–	–	No diff	CRT 16.2% RT 16.5%	2 ^b	66 ^b	–
Pearcey [27]	No	–	–	–	–	–	–	CRT 6% RT 12%	6.6	102.8	65
Hongwei [15]	Yes	3	2 + 3	–	–	–	No diff	–	–	–	–
Wong 89 [44]	No	–	–	–	–	–	–	–	42	72	–
Lira Puerto [20]	No	–	–	–	–	–	–	–	–	–	–
Fernandez [10]	No	–	–	–	–	–	–	–	17	48	25
Hernandez [14]	No	–	–	–	–	–	–	–	2	49	27
Lorvidhaya [21]	No	–	–	–	–	–	–	–	15	59	25
Roberts [31]	No	–	–	–	–	–	–	–	–	–	–
Singh [35]	No	–	–	–	–	–	–	–	12 [?]	?	?
Thomas [37]	Yes	–	–	–	–	–	No diff	–	?	?	59
Wong 99 [45]	Yes	–	–	2	1234	–	No diff	–	12	130	66/96
Leborgne	Yes	–	–	–	–	–	No diff	–	3	51	27

^a Estimated from median and recruitment.

^b From censoring or numbers at risk on survival curve.

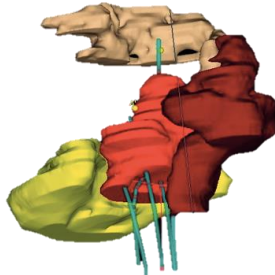
STANDARD OF CARE



45/50 Gy in 25 sessions of 1,8/2 Gy



Weekly Cisplatin 40 mg/m²



Brachytherapy

Duration

Authors	N	Total duration time of treatment	Local control consequences
Petereit ¹	202	55 days	↓ 0.7 % /d
Perez ²	1224	49 days	↓ 0.85 % /d
Girinsky ³	386	52 days	↓ 1.1 % /d
Mazeron ⁴	225	56 days	↓ 0.63 % /d
Tanderup ⁵	485	49 days	↓ 0.28 % /d

1. Petereit DG, et al. *IJROBP*, 1995.
2. Perez CA, et al. *IJROBP* 1995
3. Girinsky T, et al. *IJROBP* 1993.
4. Mazeron R, et al. *Radiother Oncol* 2015
5. Tanderup K, et al. *Radiother Oncol* sept 2016;

EDITORIAL

Curative Radiation Therapy for Locally Advanced Cervical Cancer: Brachytherapy Is NOT Optional

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Richard Pötter, MD,^{||} and Perry W. Grigsby, MD^{*}

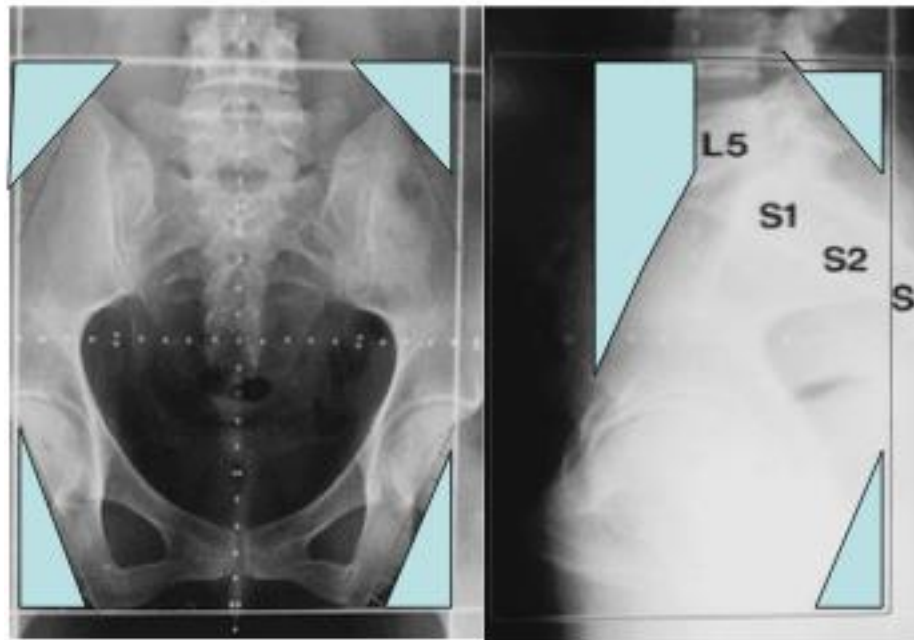
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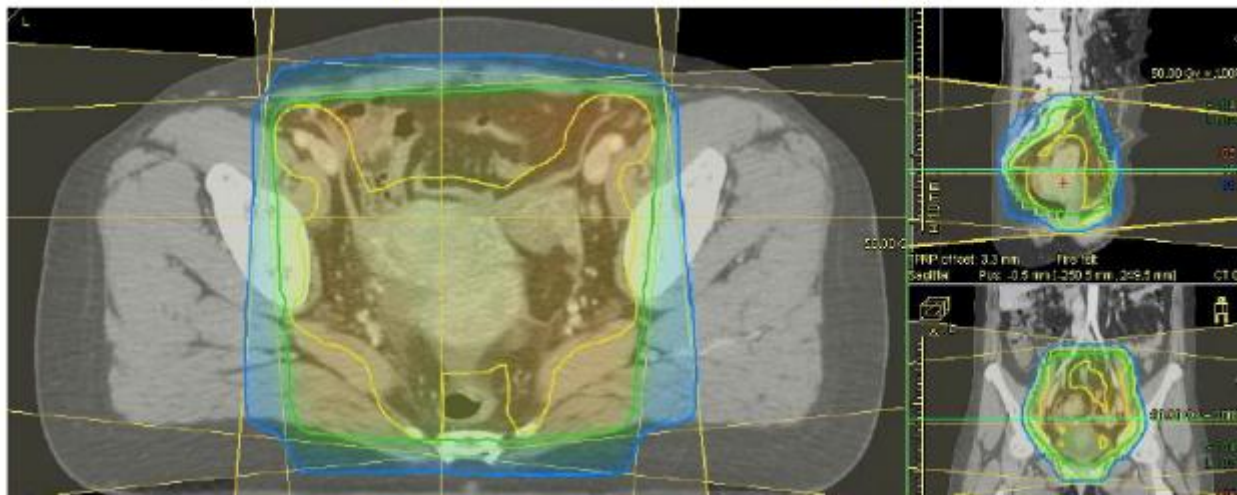
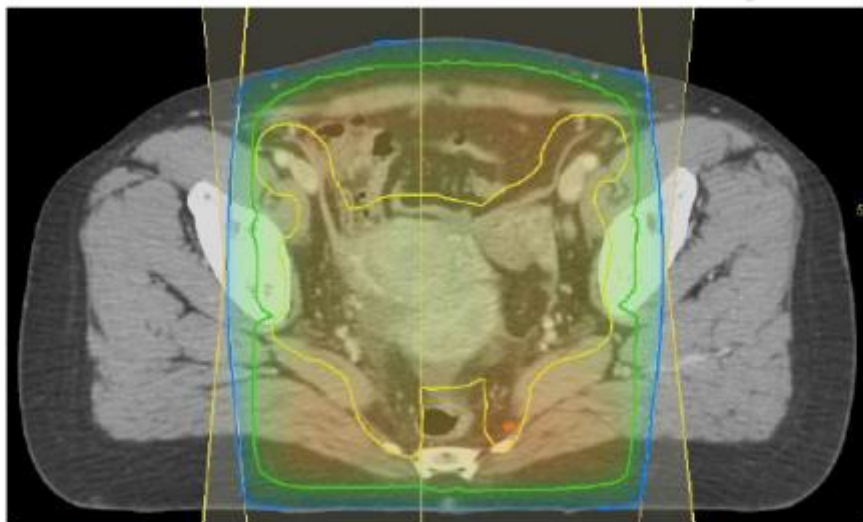
From 2D to 3D

- Significant decrease of % volume for OAR receiving more than 70% of prescribed dose :

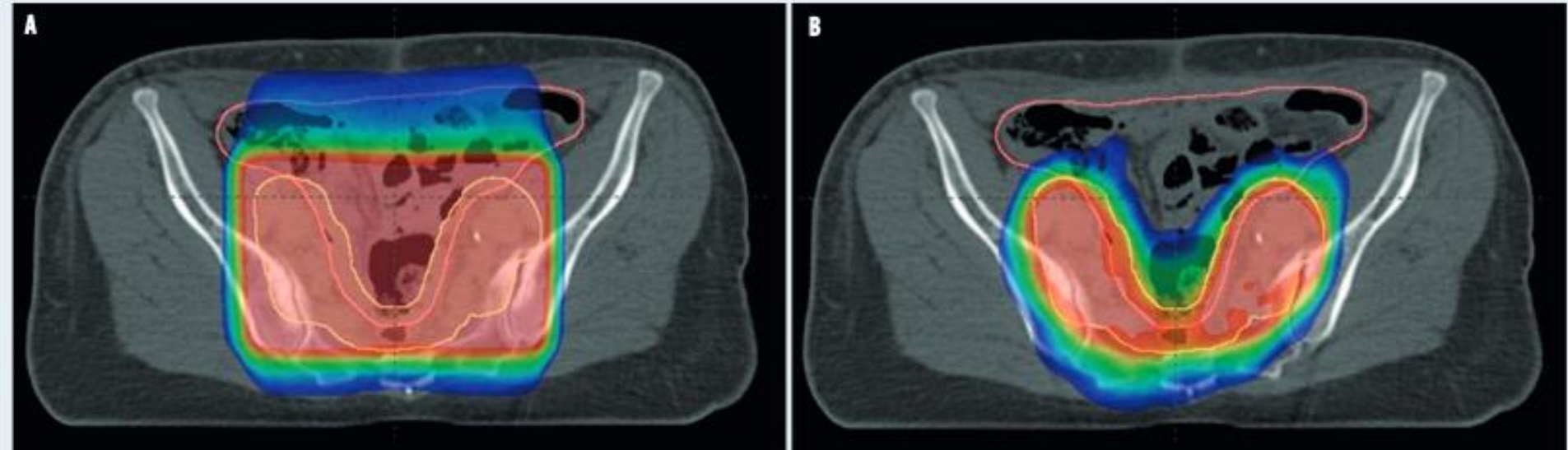
- 34% for bladder volume
- 15% of bowell

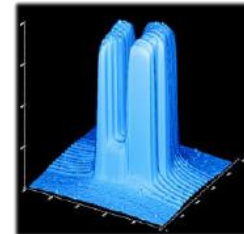
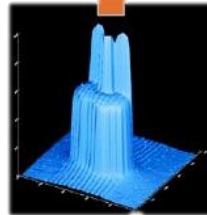
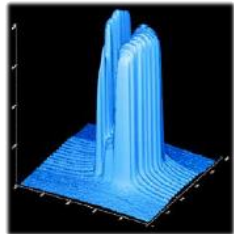
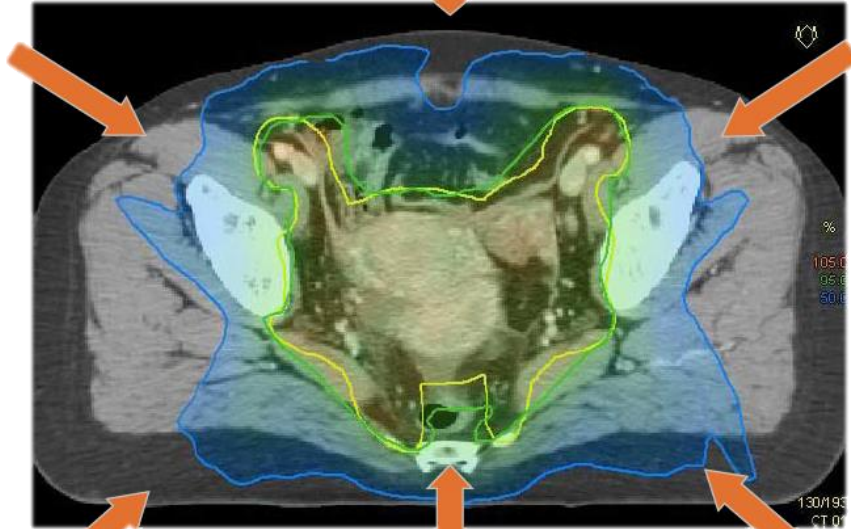
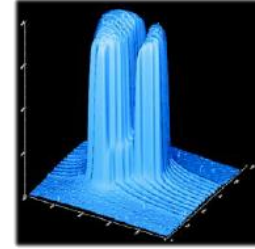
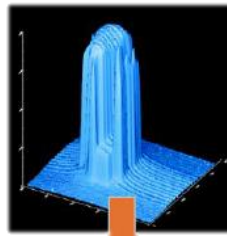
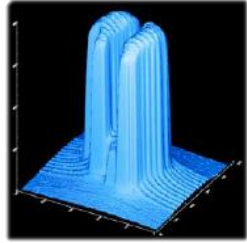


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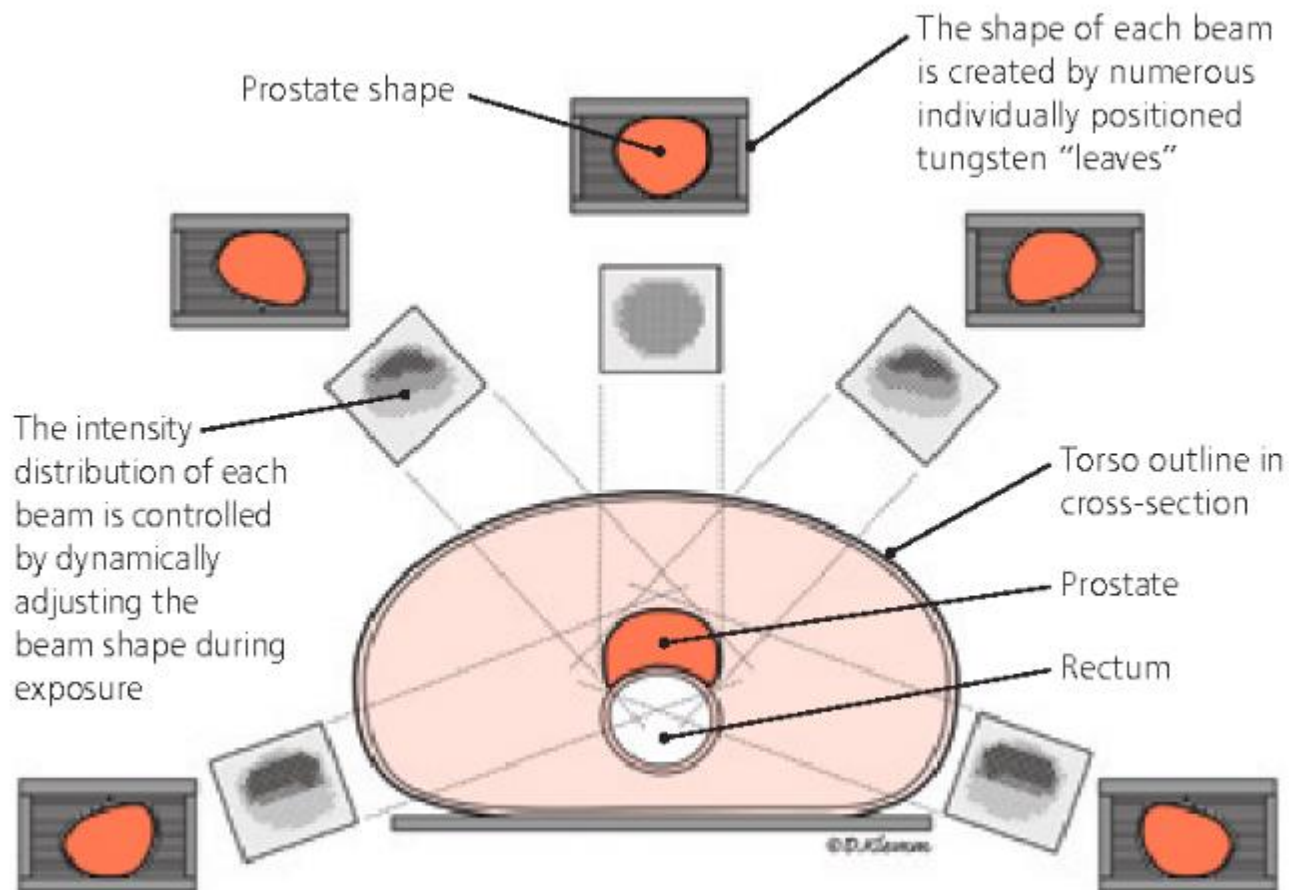


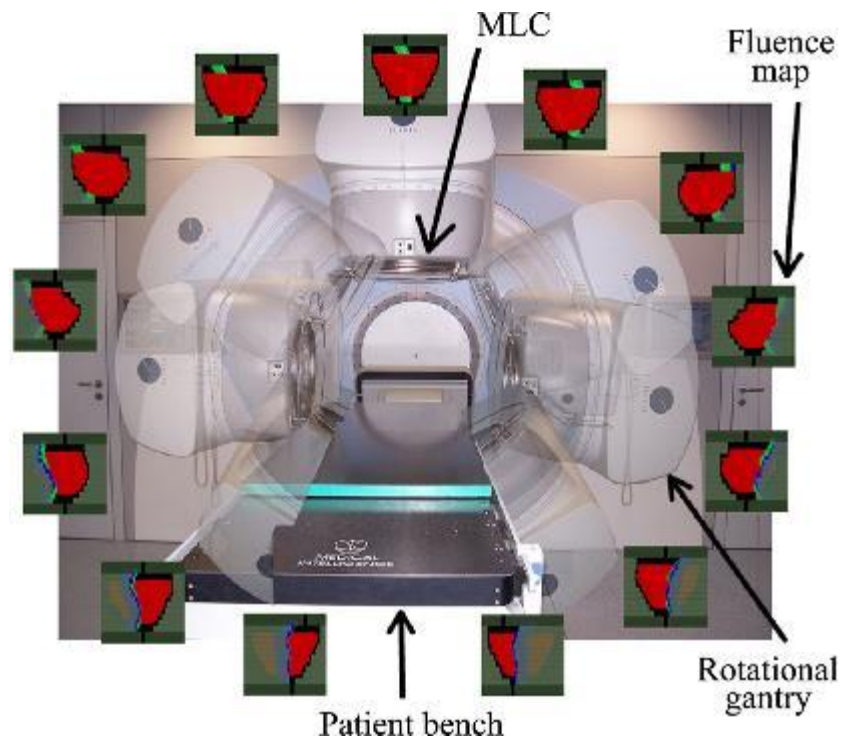
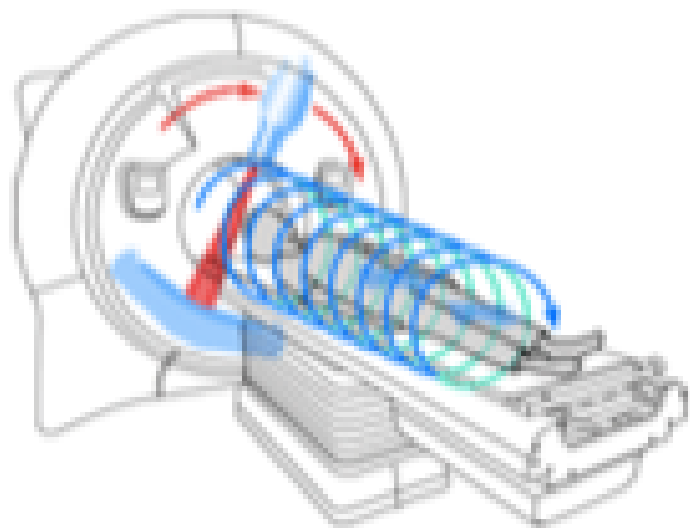
From 3D to IMRT

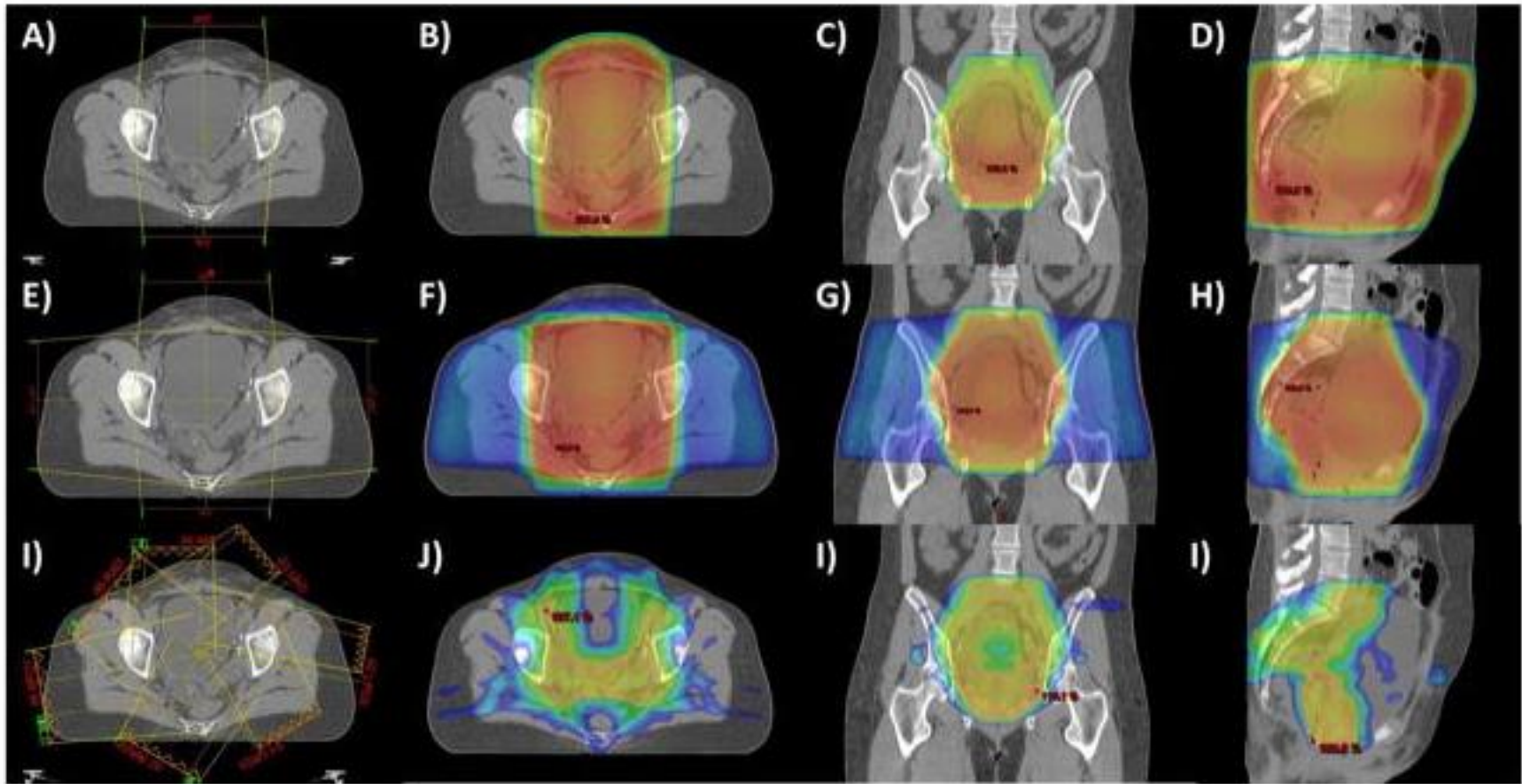




Intensity-Modulated Radiation Therapy







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RESEARCH

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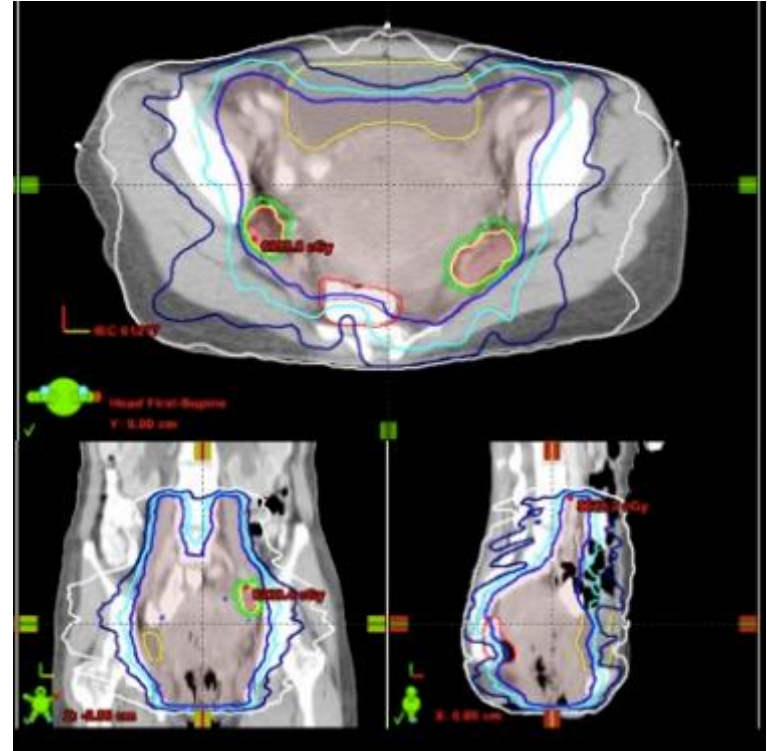
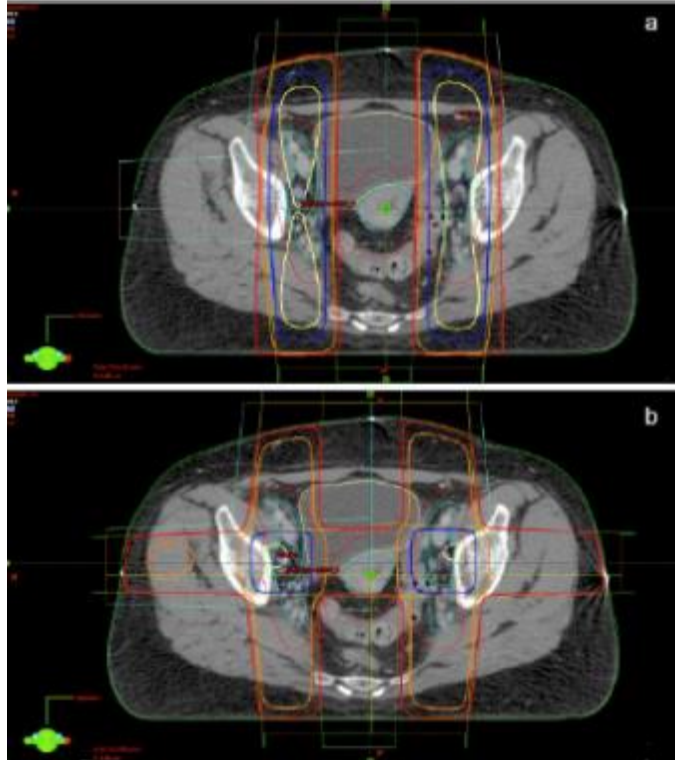
Dosimetric comparison of intensity modulated
radiotherapy and three-dimensional conformal
radiotherapy for patients with
prostate cancer: a systematic
meta-analysis

Baojuan Yang^{1†}, Lin Zhu^{2†}, Haiyan Cheng¹, Qi Li¹, Yunyan Zhang^{1*} and Yashuang Zhao²

IMRT significantly reduced
the % volume of
rectum and small bowel

Not significant for
bladder and bone
marrow

Sequential or simultaneous lymph nodes boost



Guidelines



ESMO > Guidelines > Gynaecological Cancers > Cervical Cancer

EUPDATE – CERVICAL CANCER TREATMENT RECOMMENDATIONS

eUpdate - Cervical Cancer Treatment Recommendations

Published: 01 April 2020. Authors: ESMO Guidelines Committee

CLINICAL PRACTICE GUIDELINES | VOLUME 10, ISSUE 4, P220-234, JULY 01, 2020

Radiation Therapy for Cervical Cancer: Executive Summary of an ASTRO Clinical Practice Guideline

Junzo Chino, MD = Christina M. Annunziata, MD, PhD = Sushil Beriwal, MD, MBA = ...

Chika Nwachukwu, MD, PhD = Daniel Petereit, MD = Akila N. Viswanathan, MD, MPH = [Show all authors](#)

Published: May 18, 2020 * DOI: <https://doi.org/10.1016/j.prro.2020.04.002>

ESGO/ESTRO/ESP GUIDELINE | VOLUME 127, ISSUE 3, P404-416, JUNE 01, 2018

The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology guidelines for the management of patients with cervical cancer

David Cibula = Richard Pötter = François Panchamp = ... Karl Tamussino = Pauline Wimberger = Maria Rosaria Raspollini = [Show all authors](#)

Published: May 01, 2018 * DOI: <https://doi.org/10.1016/j.radonc.2018.03.003>



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journal homepage: www.elsevier.com/locate/ejogrb


Review article

British Gynaecological Cancer Society (BGCS) cervical cancer guidelines: Recommendations for practice

Nick Reed^{a,*}, Janos Ballega^b, Tara Barwick^c, Lynn Buckley^d, Kevin Burton^e, Gemma Eminowicz^f, Jenny Forrest^g, Raji Ganesan^h, Rosie Harrand^g, Cathrine Hollandⁱ, Tamara Howe^l, Thomas Ind^k, Rema Iyer^l, Sonali Kaushik^{mn}, Robert Music^o, Azmat Sadozye^a, Smruta Shanbhag^o, Nadeem Siddiqui^g, Sheeba Syed^{pl}, Natalie Percival^q, Natasha Lauren Whitham^r, Andy Nordin^g, Christina Fotopoulou^l

The European Society of Gynaecological Oncology/European Society for Radiotherapy and Oncology/European Society of Pathology guidelines for the management of patients with cervical cancer

David Cibula   • Richard Pötter • François Planchamp • ... Karl Tamussino • Pauline Wimberger •
Maria Rosaria Raspollini • [Show all authors](#)

Published: May 01, 2018 • DOI: <https://doi.org/10.1016/j.radonc.2018.03.003> •  Check for updates

Definitive Chemoradiotherapy

- External beam radiotherapy is recommended minimum as 3-dimensional (3D) conformal radiotherapy. The preferred treatment is intensity-modulated radiotherapy (IMRT) because of the more conformal dose distribution that maximizes sparing of organs at risk.
- External beam radiotherapy can be applied as concomitant chemoradiotherapy with total dose of 45 to 50 Gy (1.8 Gy per fraction) and single-agent radiosensitizing chemotherapy,
- Boost treatment for involved lymph node(s) may be applied as simultaneous integrated boost within the IMRT treatment or as sequential boost. The total dose including the contribution from brachytherapy should be 55 to 60 Gy (equieffective dose to 2 Gy per fraction [EQD2]). An alternative treatment option is surgical debulking of enlarged nodes.
- Image-guided radiotherapy (IGRT) is recommended for IMRT to ensure safe dose application in the tumor-related targets, to account for motion uncertainties, to reduce margins, and to achieve reduced doses to organs at risk.
- Overall treatment time for EBRT should not exceed 5 to 6 weeks.

Take home messages

- Main part of the treatment for cervix cancers from FIGO stages IB2 – IV
- IMRT recommended
- Integrated boost in order to limit overall duration treatment time