Incontri Bresciani di Radioterapia Oncologica – Edizione 2013

DIFFICULT CLIMBING: TREATMENT OF GLIOMAS AND A TRIBUTE TO G.P. BITI

Brescia – October 3rd /4th, 2013

Riccardo Santoni MD
Università degli Studi di Roma "Tor Vergata

Gynecologic Cancer: a radiation oncology perspective

Perspectives

I have a Dream about the Radiation Oncology perspectives on gynaecological tumours and the Competitors on this subject:

1 – To strongly state which are the "best" up-to-date treatments to offer to each single patient without being told or ordered by others!

2 – To reduce the uncertainties and to oppose fanciful "new" treatment proposals lacking in strong clinical evidence!

3 – To introduce in the clinical practice any reasonable innovation to improve the results and reduce acute and late toxicity.

4 – To enter as "leading actors" any reasonable research program to improve clinical results and better understand the "secrets" of gynecological tumors

5 – Not to put ***"on sale"*** our extremely large experience and knowledge in the treatment of gynecological tumors!

Carcinoma of the Cervix Uteri.
26° Annual Report

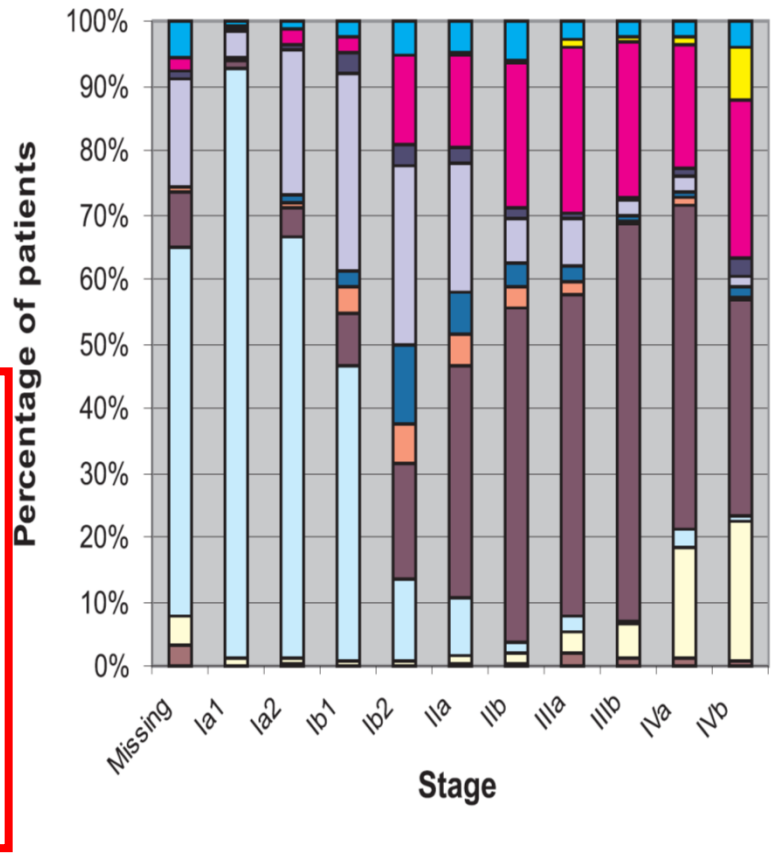
A TRIBUTE TO PROF. S.M. Magrini too!

MA QUINN, JL BENEDET, F ODICINO, P MAISONNEUVE, U BELLER, WT CREASMAN, APM HEINTZ, HYS NGAN and S PECORELLI.

Italy	Brescia (SM Magrini)	73	–	15	41	10	7
	Brescia (S Pecorelli)	65	–	43	12	2	8
	Latina (F Maneschi)	7	–	5	2	–	–
	Trento (E Arisi)	18	–	13	4	–	1

Carcinoma of the cervix uteri: Review of the 5-year survival rates reported in volumes 18–26

Vol.	Year	Patients	Survival (%)
18	1973–75	34178	55.7
19	1976–78	32428	55.0
20	1979–81	31543	53.5
21	1982–86	32052	59.8
22	1987–89	22428	65.0
23	1990–92	12153	65.4
24	1993–95	11709	72.2
25	1996–98	10525	69.9
26	**1999–2001**	**15081**	**69.6**
Total		**202097**	



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Stage	Patients (n)	Mean age (yrs)	Overall survival (%) at					Hazards ratio[a] (95% CI)
			1 year	2 years	3 years	4 years	5 years	
Ia1	829	44.5	99.8	99.5	98.3	97.5	97.5	0.2 (0.1–0.3)
Ia2	275	45.4	98.5	96.9	95.2	94.8	94.8	0.4 (0.3–0.7)
Ib1	3020	48.6	98.2	95.0	92.6	90.7	89.1	Reference
Ib2	1090	46.8	95.8	88.3	81.7	78.8	75.7	
IIa	1007	54.4	96.1	88.3	81.5	77.0	73.4	1.9 (1.6–2.2)
IIb	2510	53.5	91.7	79.8	73.0	69.3	65.8	2.7 (2.4–3.0)
IIIa	211	60.3	76.7	59.8	54.0	45.1	39.7	5.3 (4.3–6.5)
IIIb	2028	56.6	77.9	59.5	51.0	46.0	41.5	5.3 (4.7–5.9)
IVa	326	59.5	51.9	35.1	28.3	22.7	22.0	11.7 (9.9–13.8)
IVb	343	56.8	42.2	22.7	16.4	12.6	9.3	20.3 (17.4–23.7)

[a] Hazards ratio and 95% Confidence Intervals obtained from a Cox model adjusted for age and country

Fig. 11. Carcinoma of the cervix uteri: Patients treated in 1999–2001. Survival by FIGO stage, $n = 11639$.

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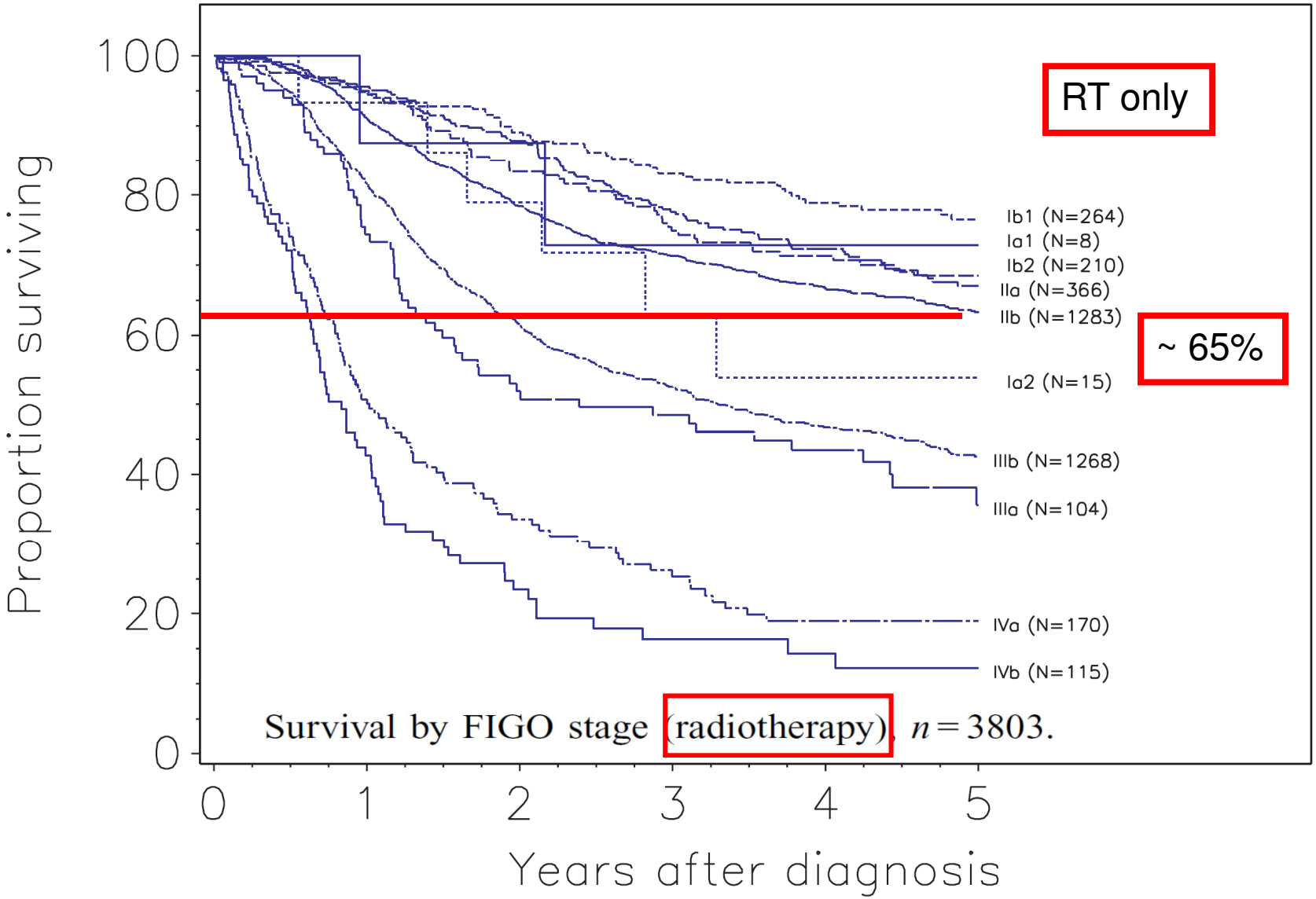

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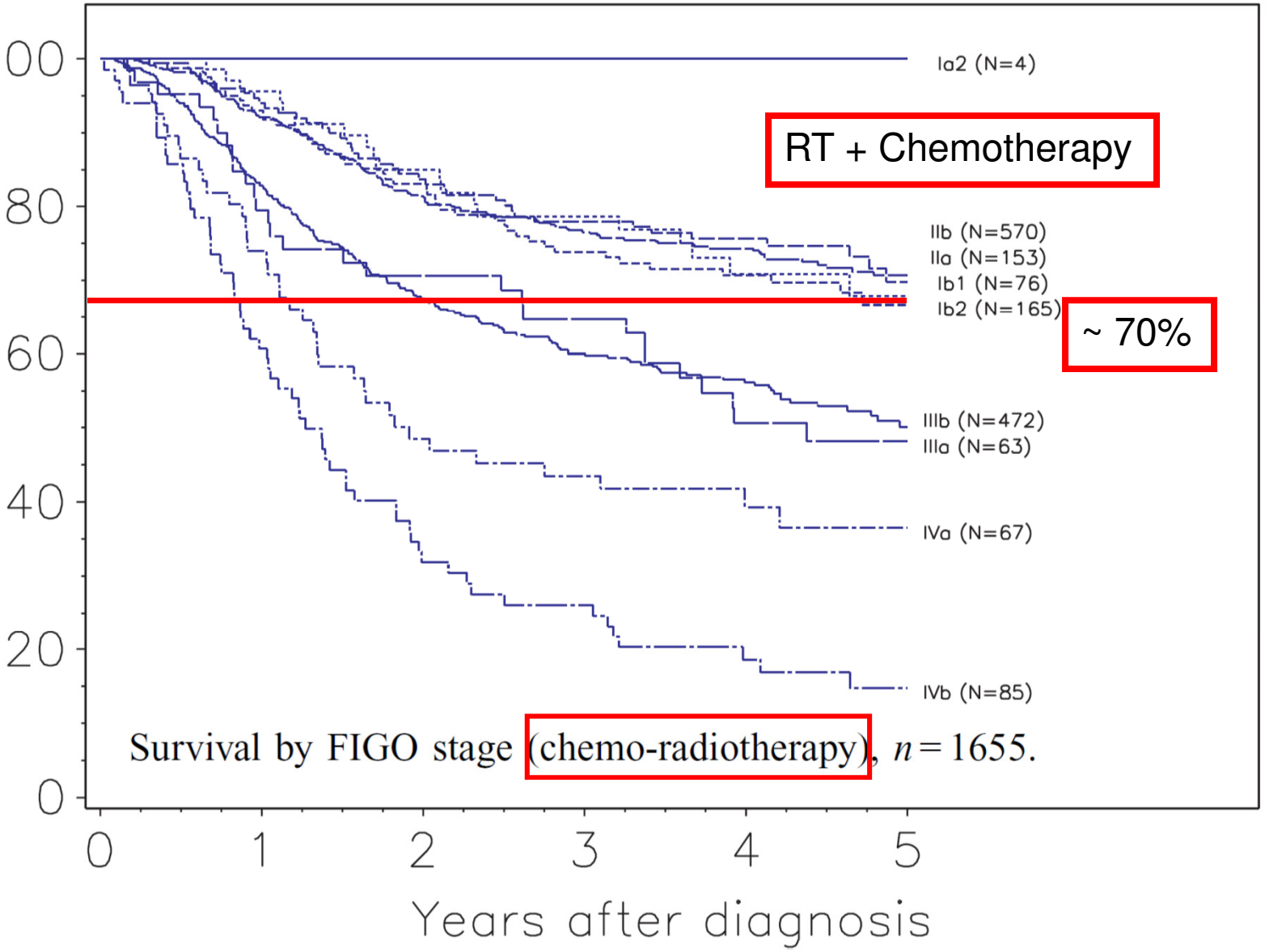
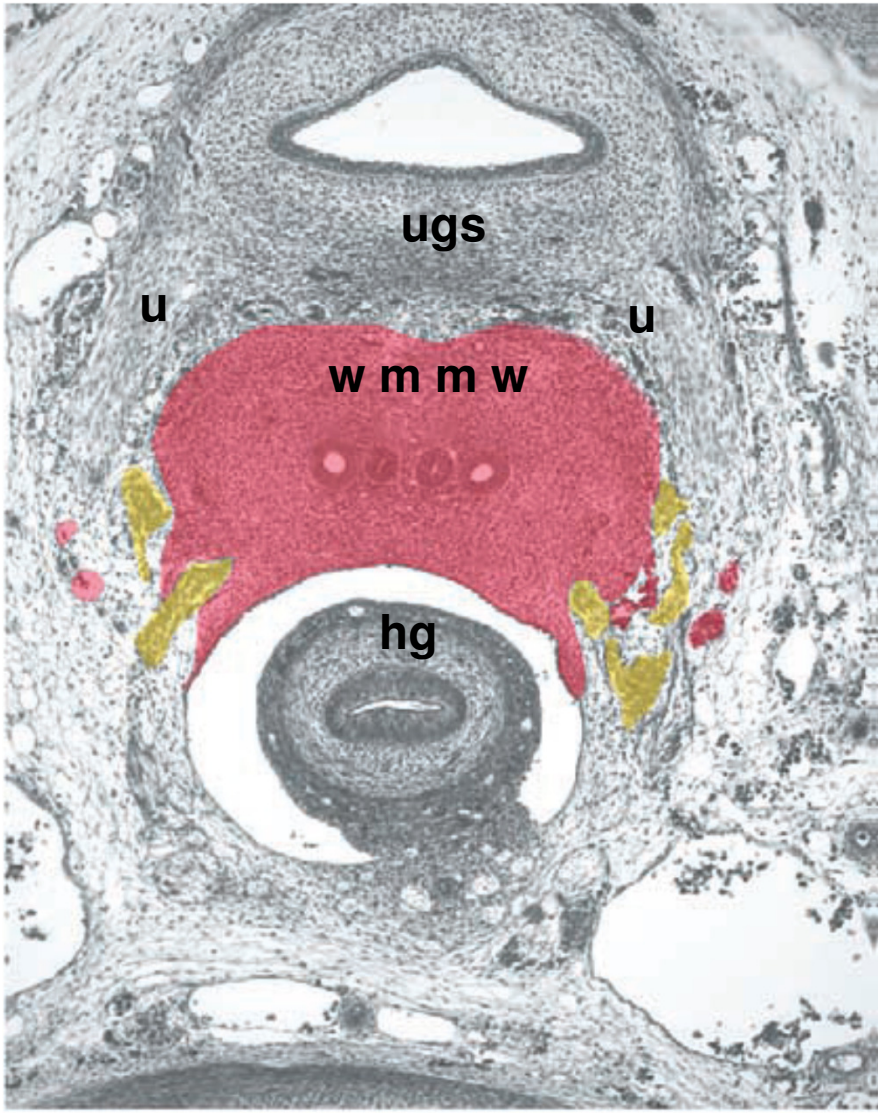


Association between the mesenchymal compartment of uterovaginal organogenesis and local tumour spread in stage IB–IIB cervical carcinoma: a prospective study
Michael Hokel, Leipzig.



Transverse sections of female embryo aged 8 weeks at the level of ureters (u) approaching the urogenital sinus (ugs)

Lancet Oncol 2005; 6: 751–56

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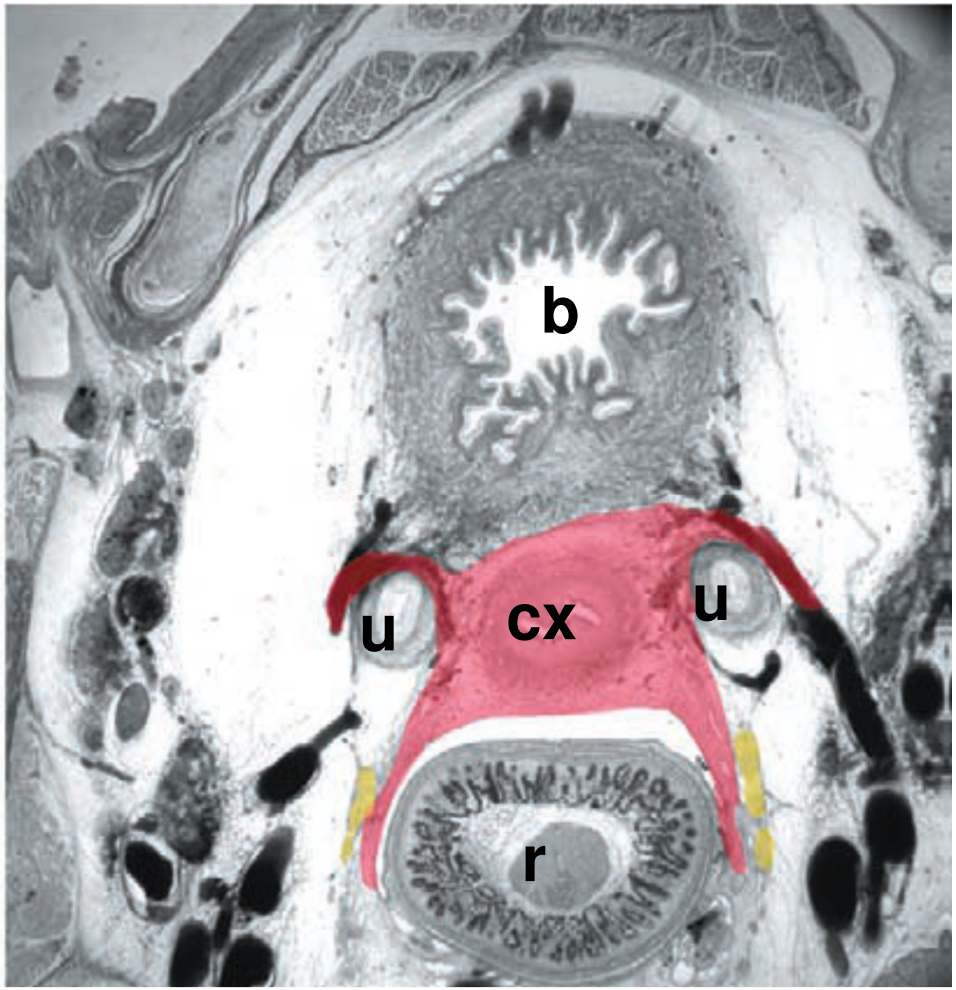


Transverse sections of a female fetus aged 24 weeks at the level of ureters (u) entering bladder (b), and of a female fetus aged 17 weeks at the level where ureters are lateral to the cervix (cx).

Lancet Oncol 2005; 6: 751–56

(Laterally) Extended Endopelvic Resection: Surgical treatment of locally advanced and recurrent cancer of the uterine cervix and vagina based on ontogenetic anatomy

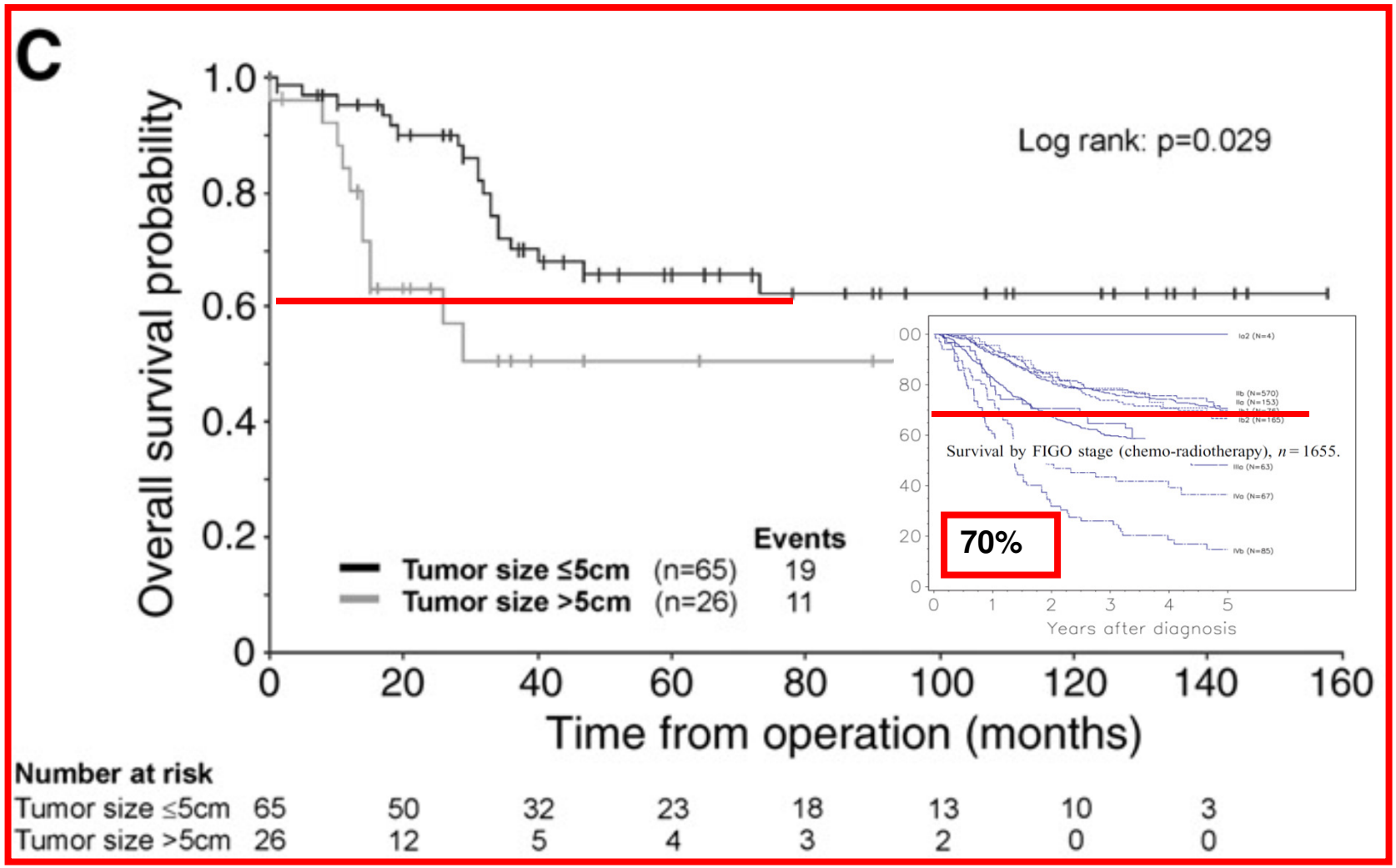
- Ontogenetic anatomy of the female pelvis provides the basis for (Laterally) Extended Endopelvic Resection ((L)EER).
- (L)EER achieves excellent local tumor control in patients with advanced and recurrent cervicovaginal cancer.

From 3/1999 to 3/2012 (13 years!) 91 consecutive patients

	Primary Carcinoma n=30	Recurrent/persistent carcinoma n=61
FIGO stages		
II (B)	9	
III (B)	11	
IV A	10	
Clinical tumor size median (range)	6 cm (3–15)	4 cm (1–8)

Gynecologic Oncology 127 (2012) 297–302

(Laterally) Extended Endopelvic Resection: Surgical treatment of locally advanced and recurrent cancer of the uterine cervix and vagina based on ontogenetic anatomy



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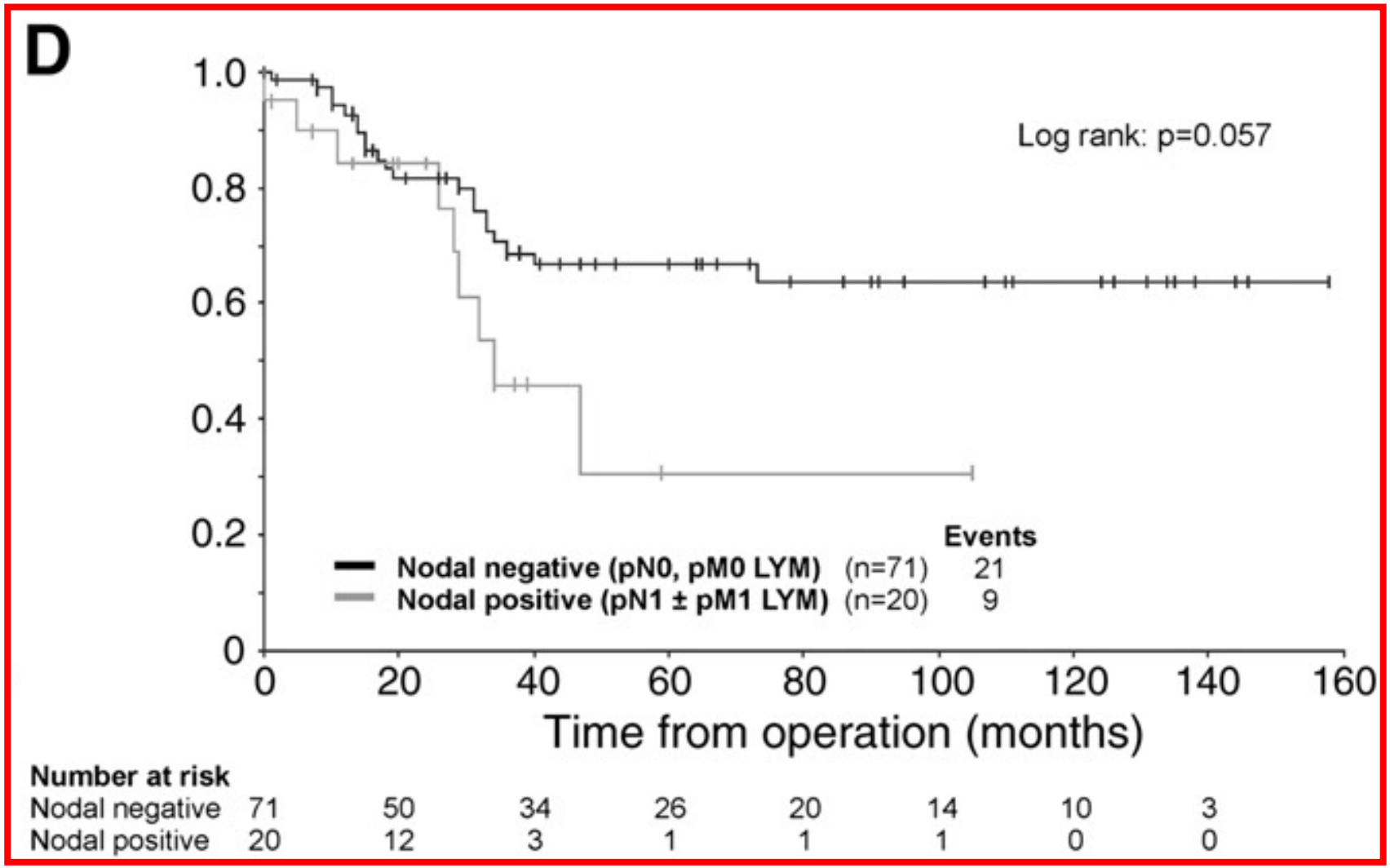

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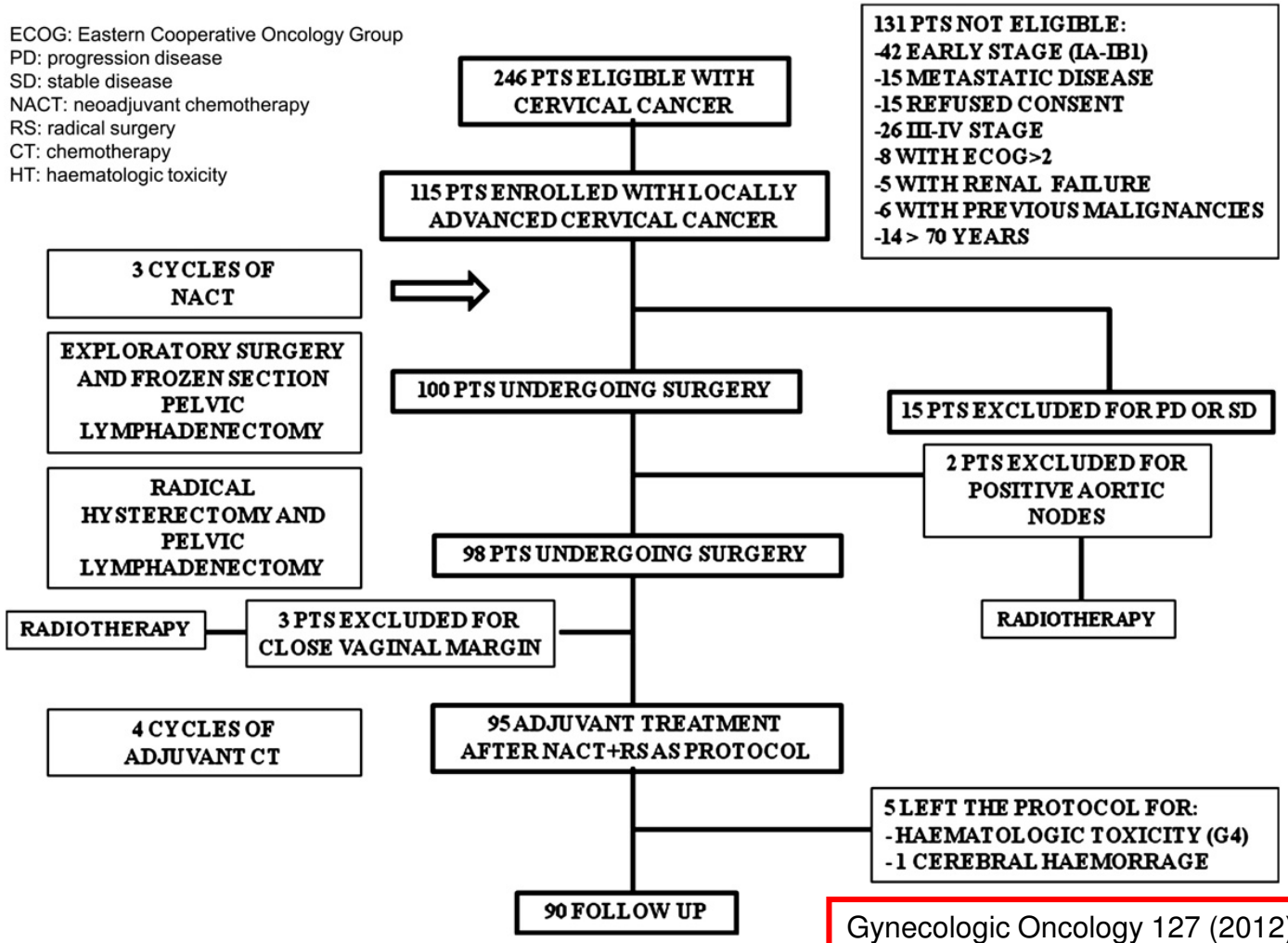
Neoadjuvant chemotherapy plus radical surgery followed by chemotherapy in Locally advanced (IB2 – IIB) cervical cancer.

Roberto Angioli a,Francesco Plotti a, Roberto Montera a, Alessia Aloisi a, Daniela Luvero a, Stella Capriglione a, Corrado Terranova a, Carlo De Cicco Nardone a, Ludovico Muzii a, Pierluigi Benedetti-Panici b



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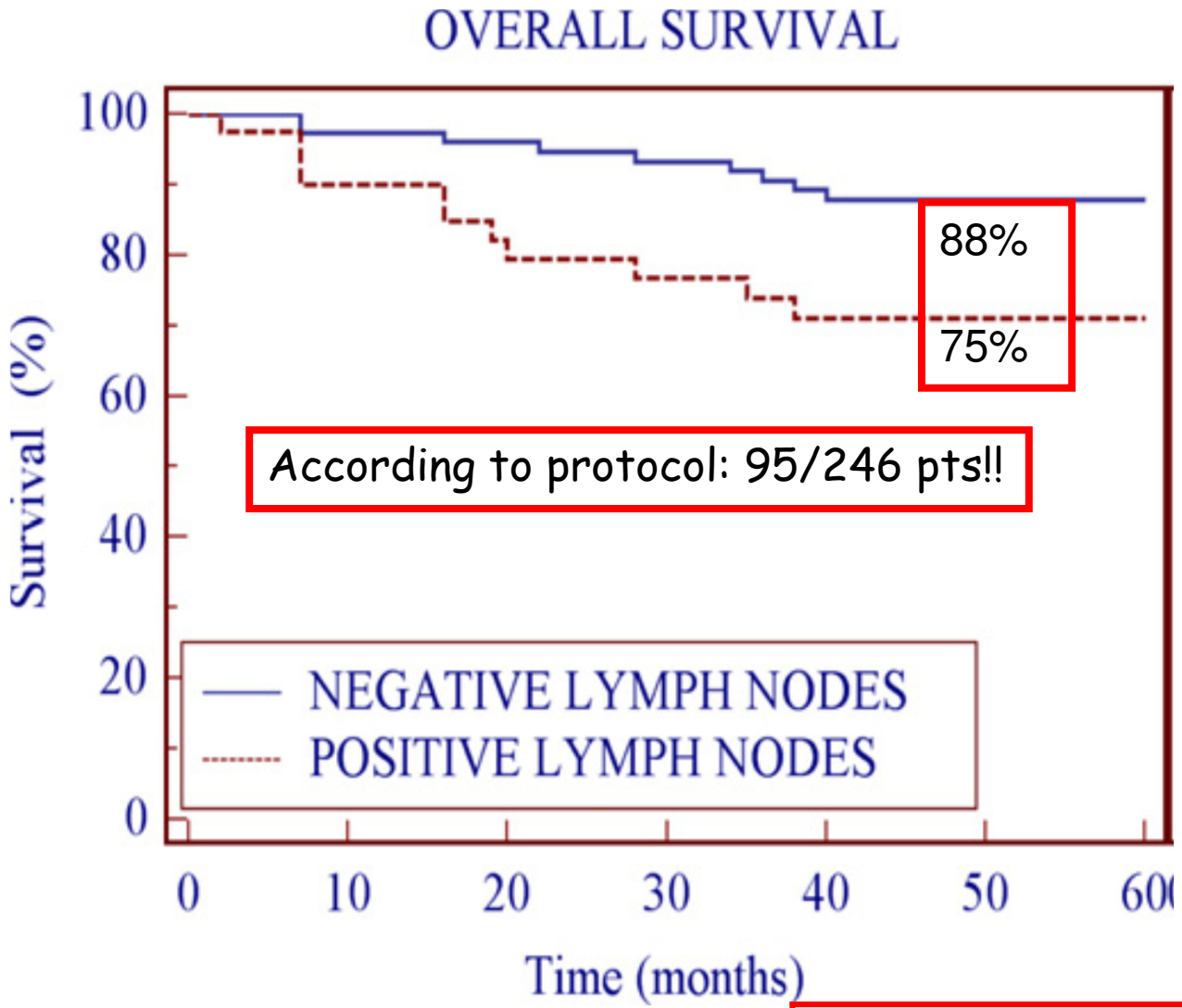

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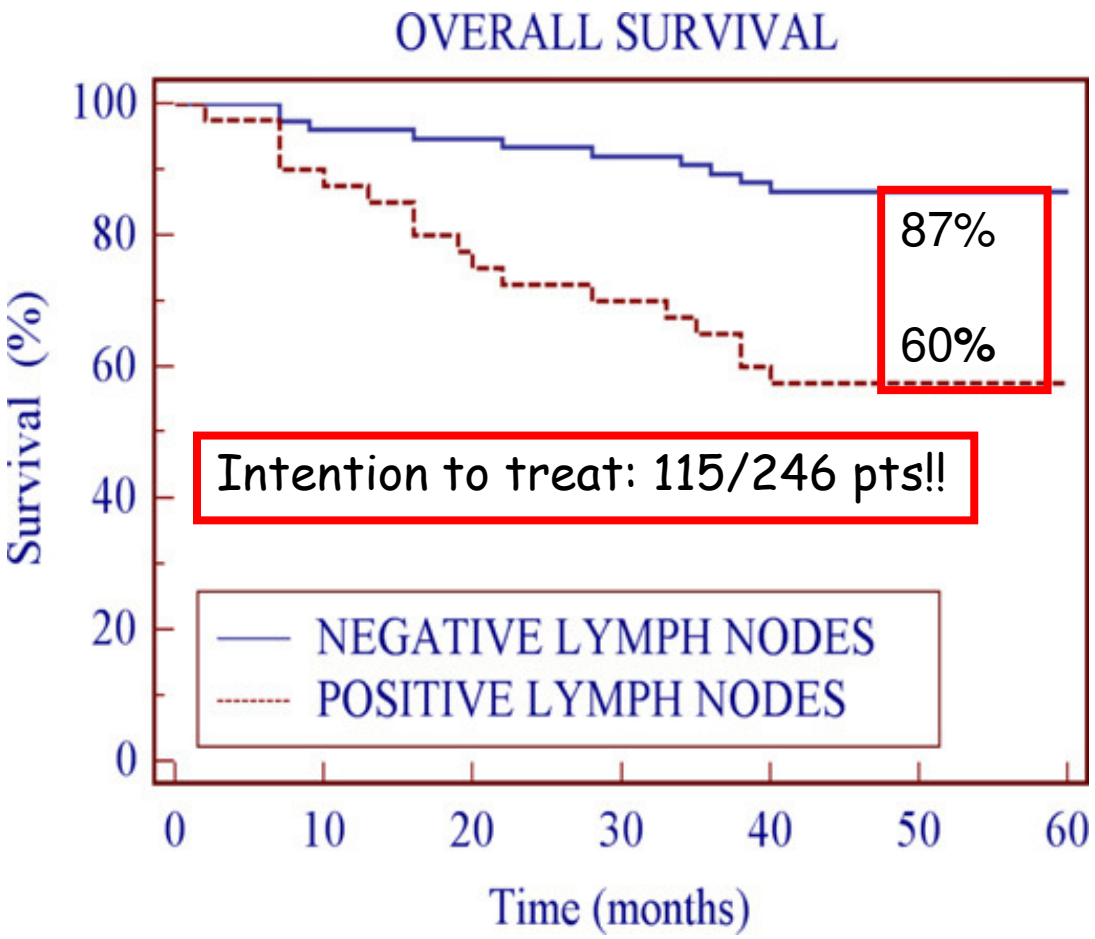

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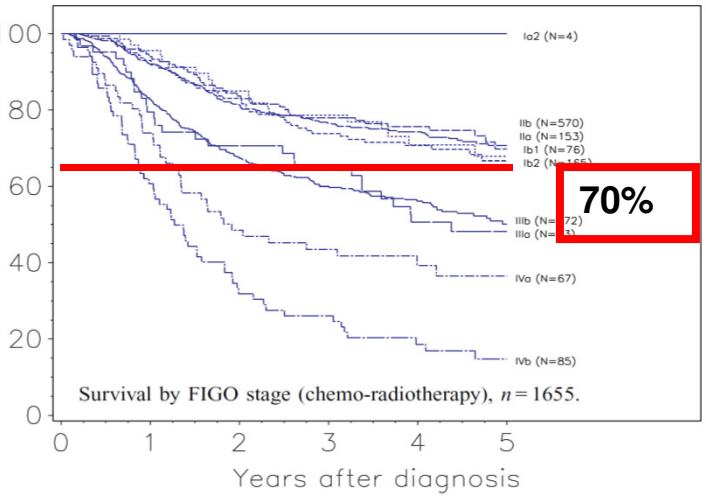

Neoadjuvant Chemotherapy and Radical Surgery Versus Exclusive Radiotherapy in Locally Advanced Squamous Cell Cervical Cancer: Results From the Italian Multicenter Randomized Study.
By Pierluigi Benedetti-Panici et al.

Do not forget that some years ago some of us were happy to join this protocol were:

1 - Radiation Therapy was delivered with sub-optimal technique and doses!
2 – Randomization was not allowed to the Radiation Oncologistis, but only to the Gynaecologists!
3 – Only one Radiation Oncologist was included among the Authors of the publication reporting on the results were similar numbers of patients were randomized between Chemotherapy + Surgery (152 patients) vs sub-optimal Radiation Therapy only (144 patients)

J Clin Oncol 20:179 -188. 2002

Neoadjuvant Chemotherapy and Radical Surgery Versus Exclusive Radiotherapy in Locally Advanced Squamous Cell Cervical Cancer: Results From the Italian Multicenter Randomized Study.
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And in spite of all these adverse to Radiation Therapy conditions:

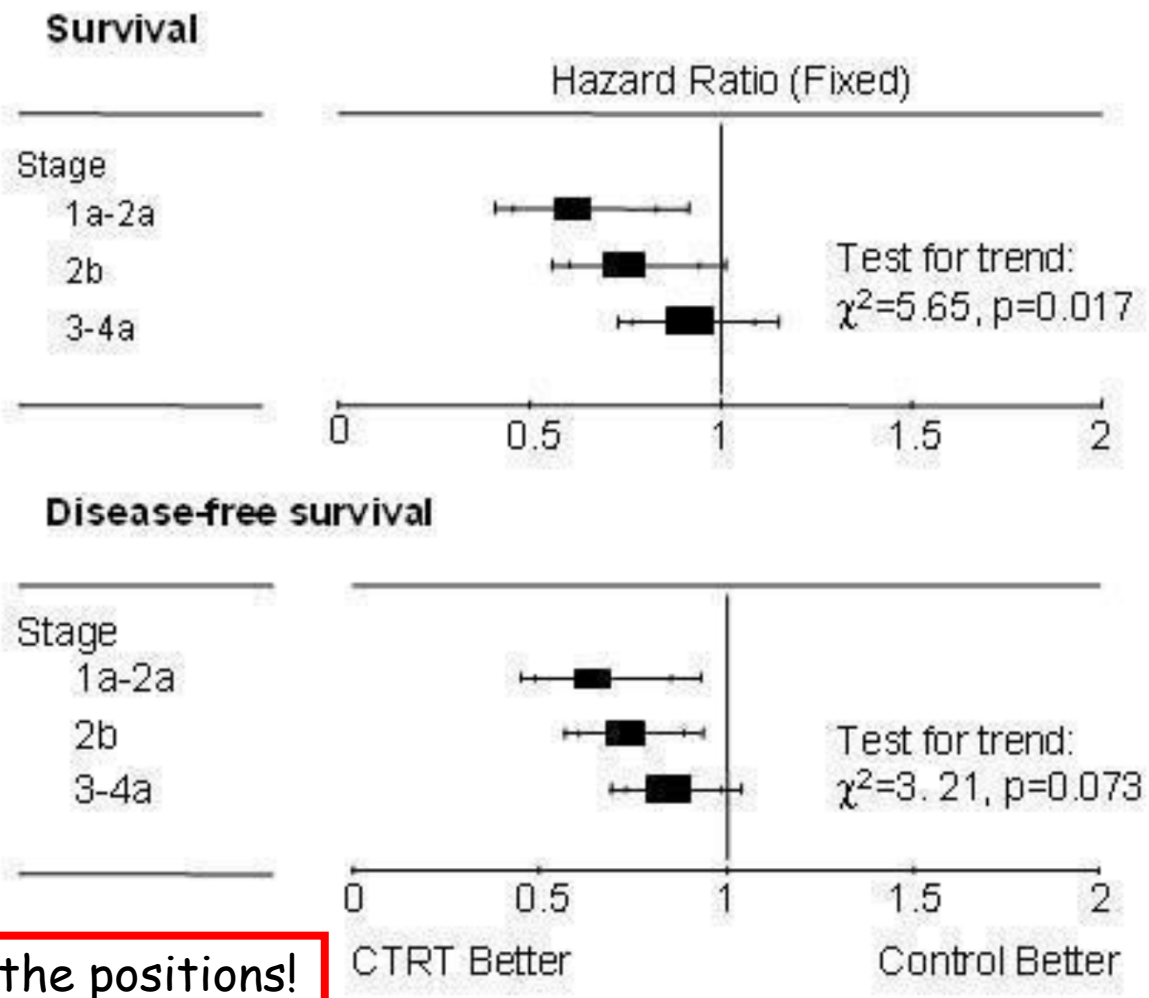
Conclusion:
Although significant only for the stage IB2 to IIB group, a survival benefit seems to be associated with the NACTRS compared with conventional RT.

J Clin Oncol 20:179 -188. 2002

Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: individual patient data meta-analysis

Cochrane Collaboration - 2010

Subgroup analysis for FIGO stage for chemoradiotherapy versus radiotherapy trials only (Overall survival and Disease-free survival)



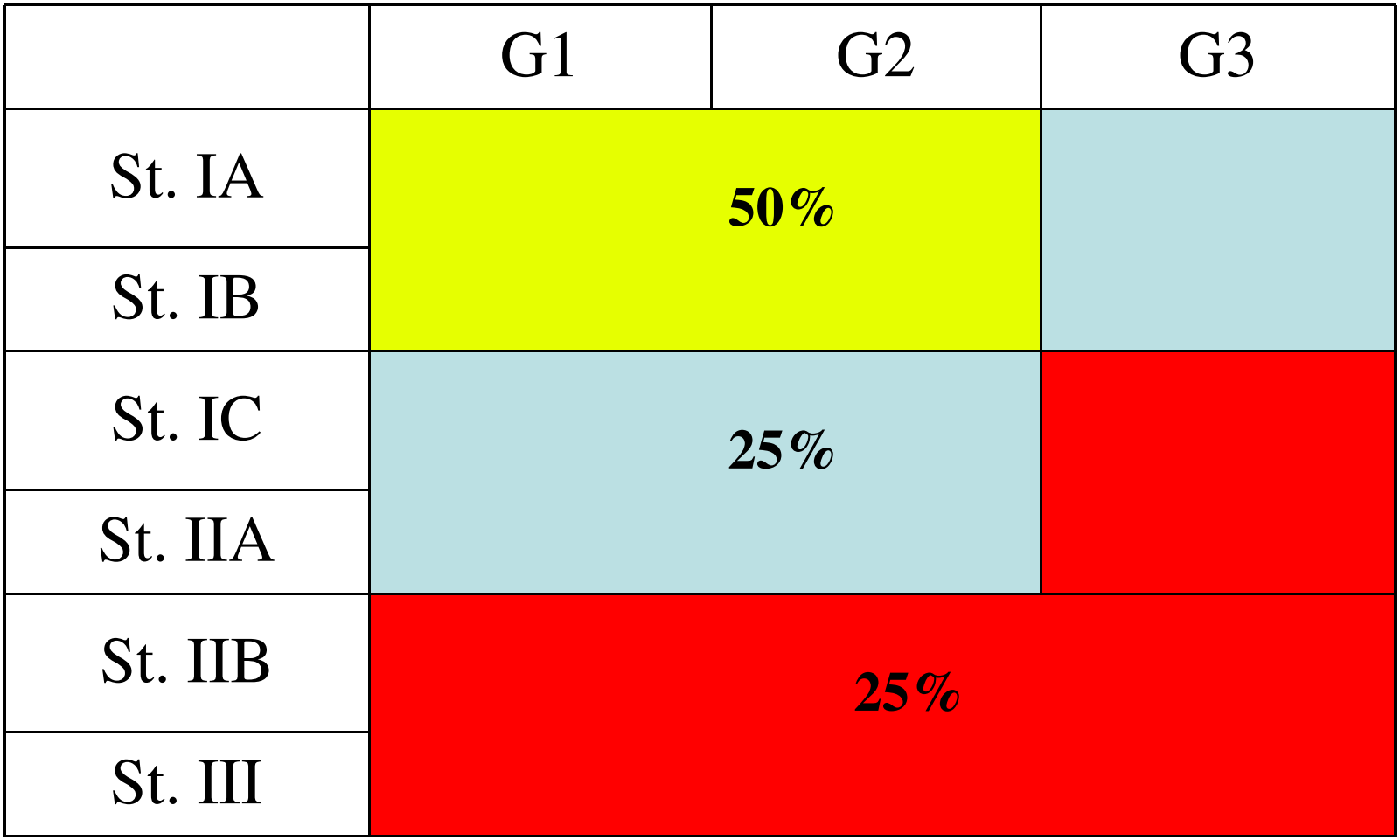
So, Please keep the positions!

Endometrial Tumours

Uterine Cancer Staging System. FIGO 2010
FIGO Annual Report on 42.000 pts - 5y survival
Pecorelli S, Int J Gynecol Obstet 2009; 103-104

	% Survival
Stage I:	75-90%
A G123, invasion < 50% myometrium:	88%
B G123, invasion > 50% myometrium:	75%
Stage II:	70%
G123, endocervix stroma	
Stage III:	45-60%
A G123, (+) serosa/adnexa:	58%
B G123, (+) vagina/parametrium:	50%
C G123, (+) nodes:	47%
IIIC1: (+) pelvic nodes	
IIIC2: (+) PAN nodes	
Stage IV:	15-20%
A G123, (+) GI, GU mucosa:	17%
B G123, distant mets + groin nodes:	15%

Endometrial Carcinoma: risk class frequency



FIGO Annual Report, Int J Gynecol Obst 83:79, 2003

Adjuvant radiotherapy for stage I endometrial cancer: systematic review and meta-analysis

Meta-analysis

In conclusion, the data showed that external beam pelvic radiotherapy should be considered in patients with multiple high-risk factors including stage 1c and grade 3 since it reduced locoregional recurrence with a trend towards reduction in deaths from all causes and endometrial cancer. However, it carries an inherent risk of damage and toxicity and should be avoided in stage 1 endometrial cancer patients with no high-risk factors.

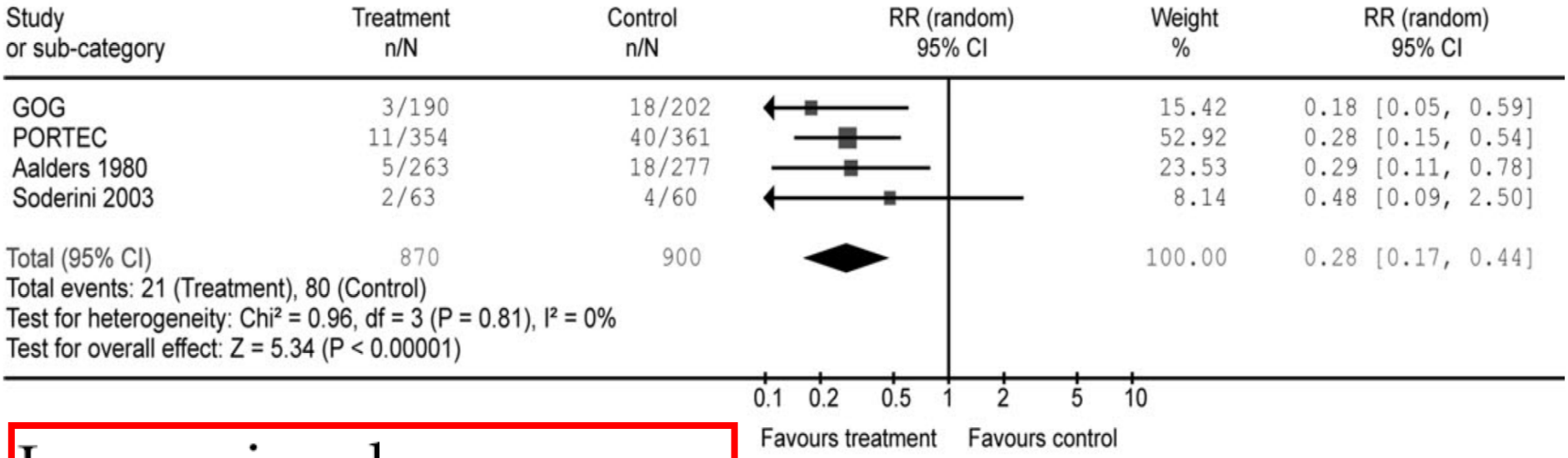
Annals of Oncology 18: 1595–1604, 2007

Adjuvant radiotherapy for stage I endometrial cancer: systematic review and meta-analysis

reduced local regional recurrence; RR of 0.28

B

Review: Adjuvant radiotherapy for stage I endometrial cancer
Comparison: 01 Figure 1: All Stage I patients: External beam radiotherapy vs. No external beam radiotherapy
Outcome: 02 Figure 1b: Locoregional recurrence



Locoregional recurrence.

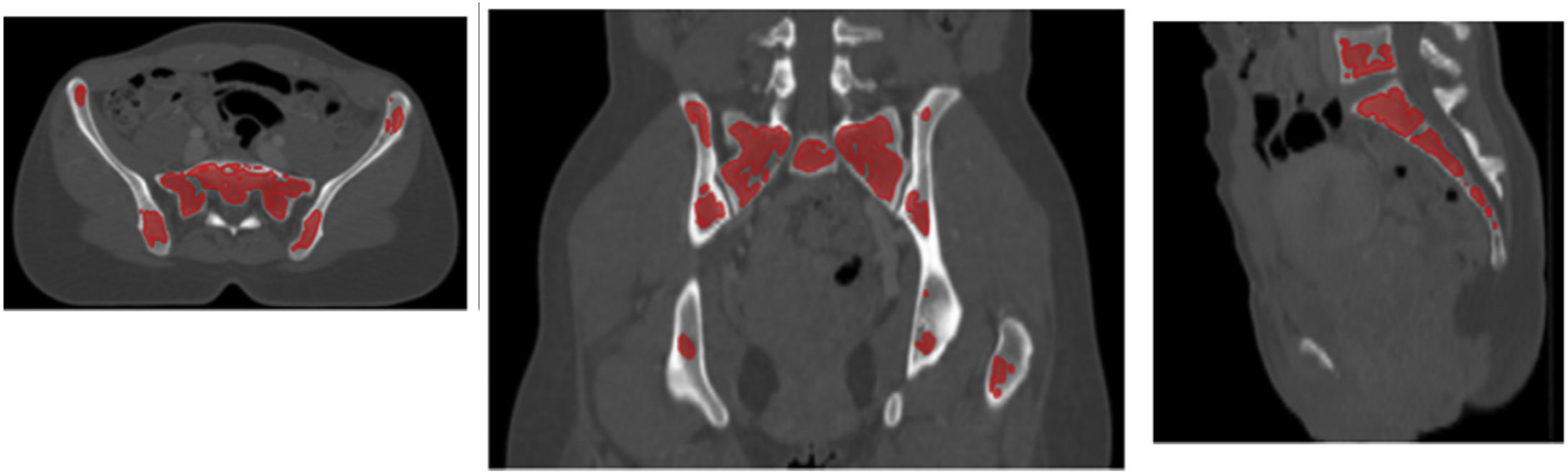
Absolute risk reduction: 6%

Annals of Oncology 18: 1595–1604, 2007

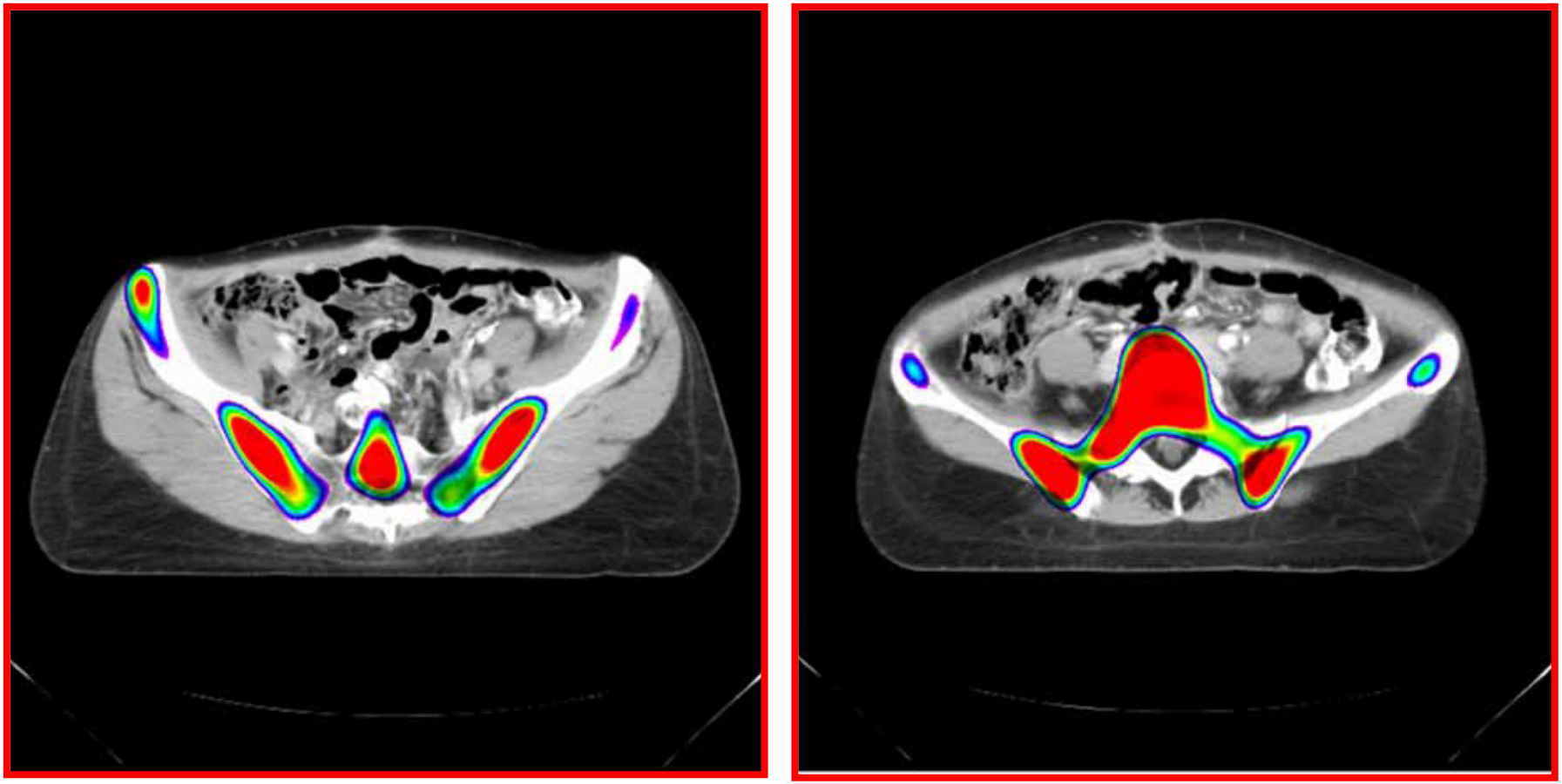
Prospective Study of Functional Bone Marrow-Sparing Intensity Modulated Radiation Therapy With Concurrent Chemotherapy for Pelvic Malignancies

Yun Liang, PhD,*,† Mark Bydder, PhD,‡ Catheryn M. Yashar, MD,*,† Brent S. Rose, MD,*,† Mariel Cornell, CMD,* Carl K. Hoh, MD,‡ Joshua D. Lawson, MD,*,† John Einck, MD,* Cheryl Saenz, MD,§ Paul Fanta, MD,‖ Arno J. Mundt, MD,*,† Graeme M. Bydder, MD,‡ and Loren K. Mell, MD*,†

*Department of Radiation Oncology, †Center for Advanced Radiotherapy Technologies, ‡Department of Radiology, §Department of Gynecologic Oncology, and ‖Division of Hematology-Oncology, University of California, San Diego, La Jolla, California



Incorporation of SPECT bone marrow imaging into intensity modulated whole-pelvic radiation therapy treatment planning for gynecologic malignancies



Radiotherapy and Oncology 77 (2005) 11–17

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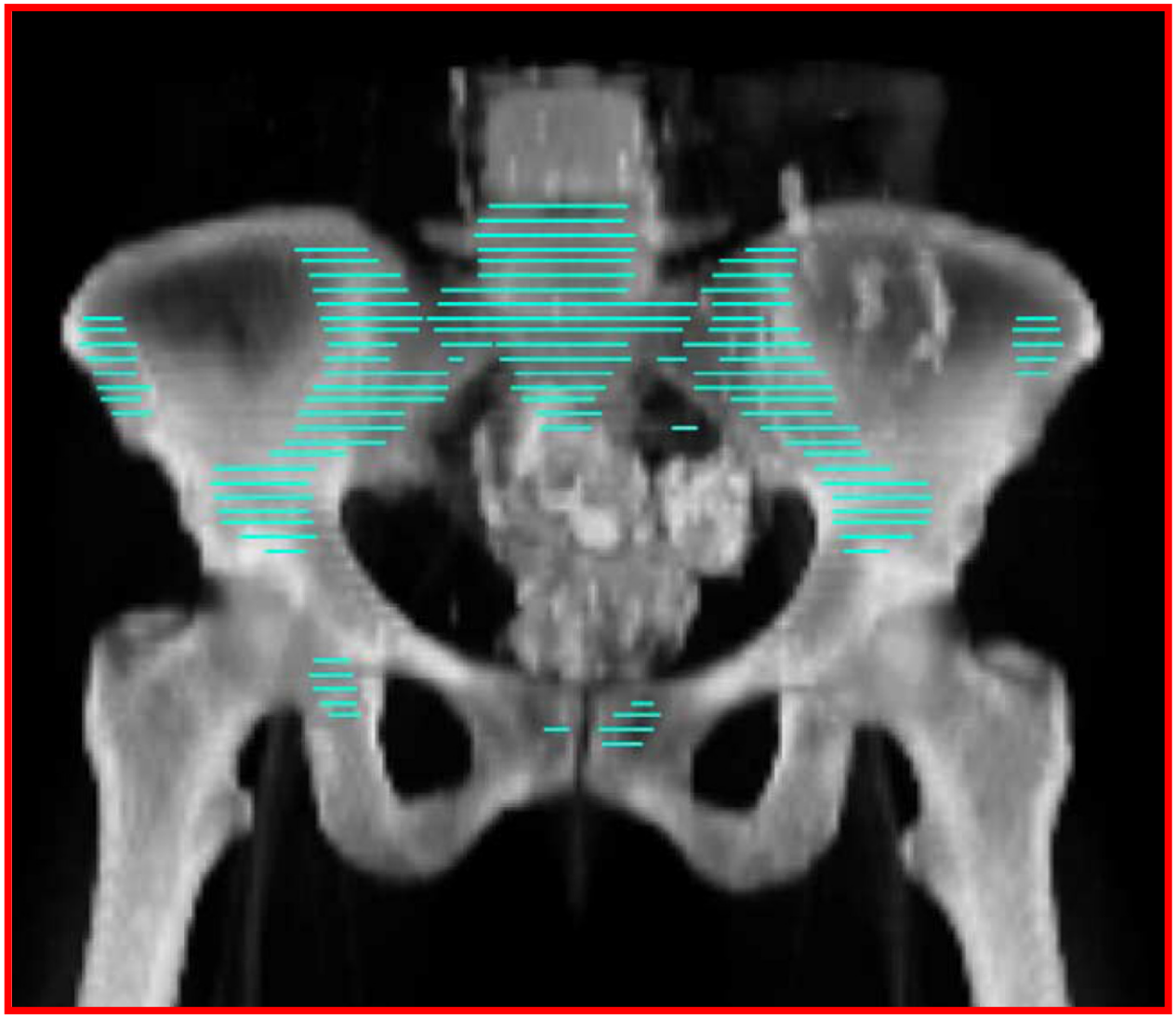

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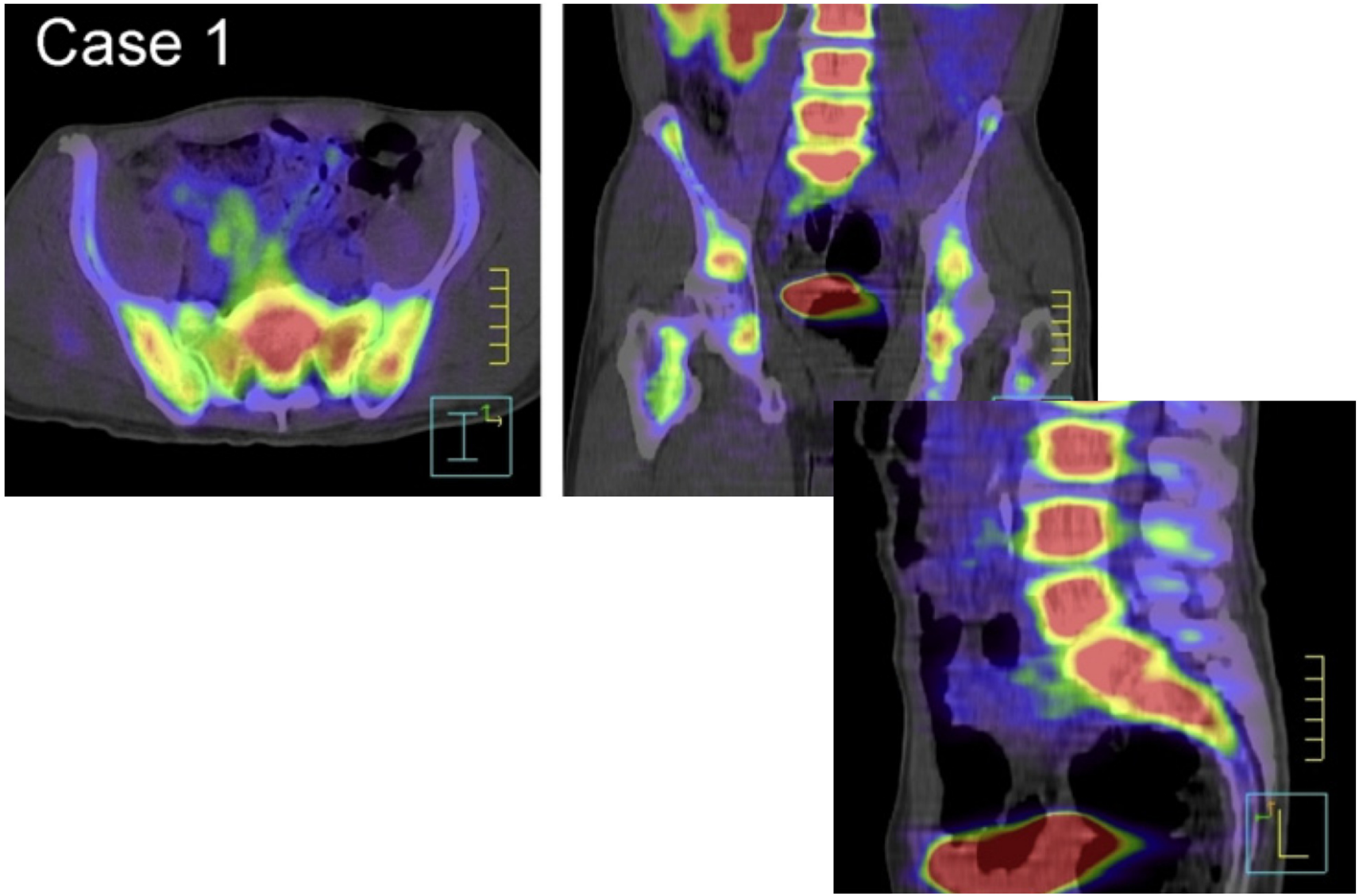
A methodology for incorporating functional bone marrow sparing in IMRT planning for pelvic radiation therapy



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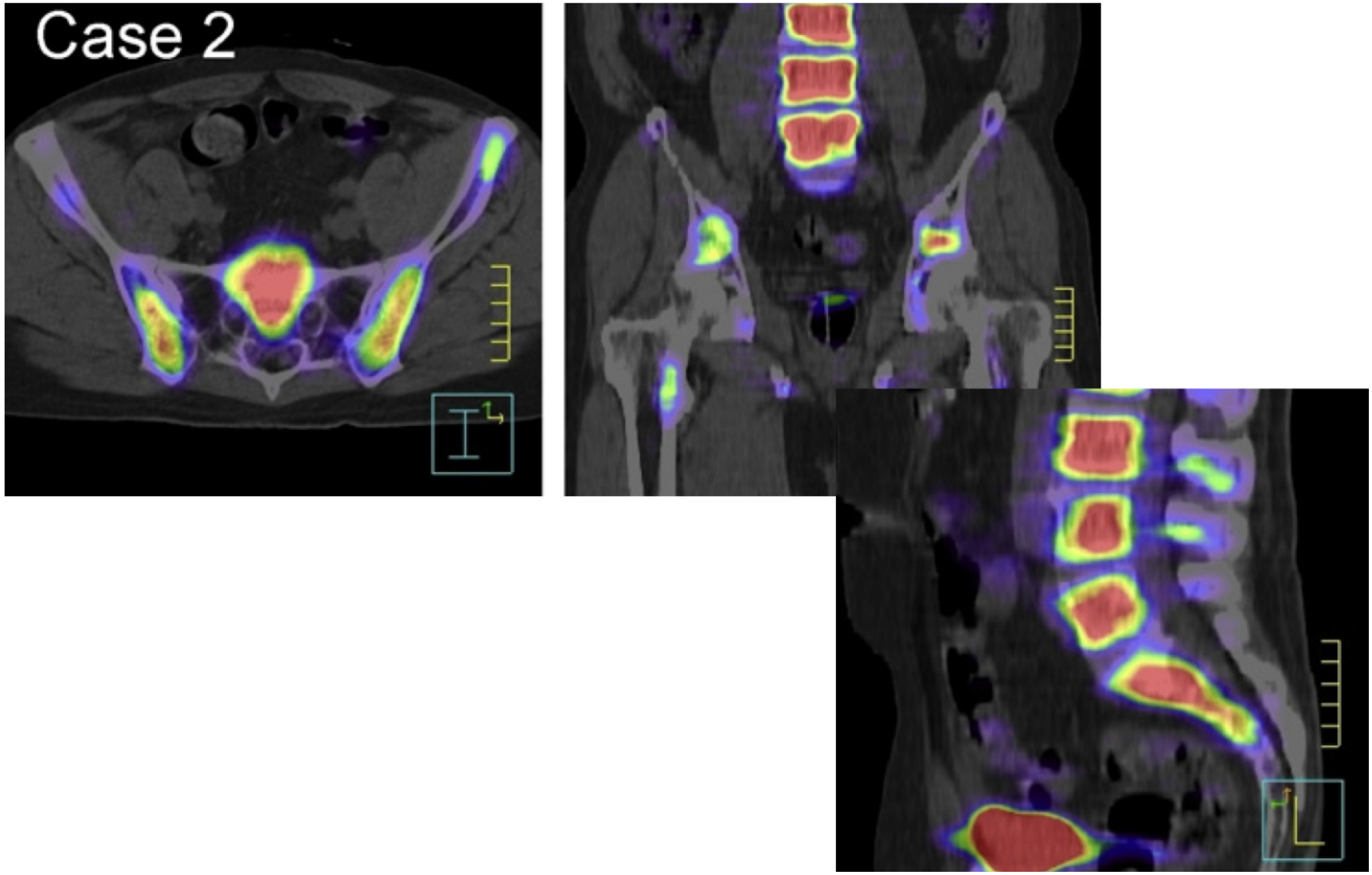

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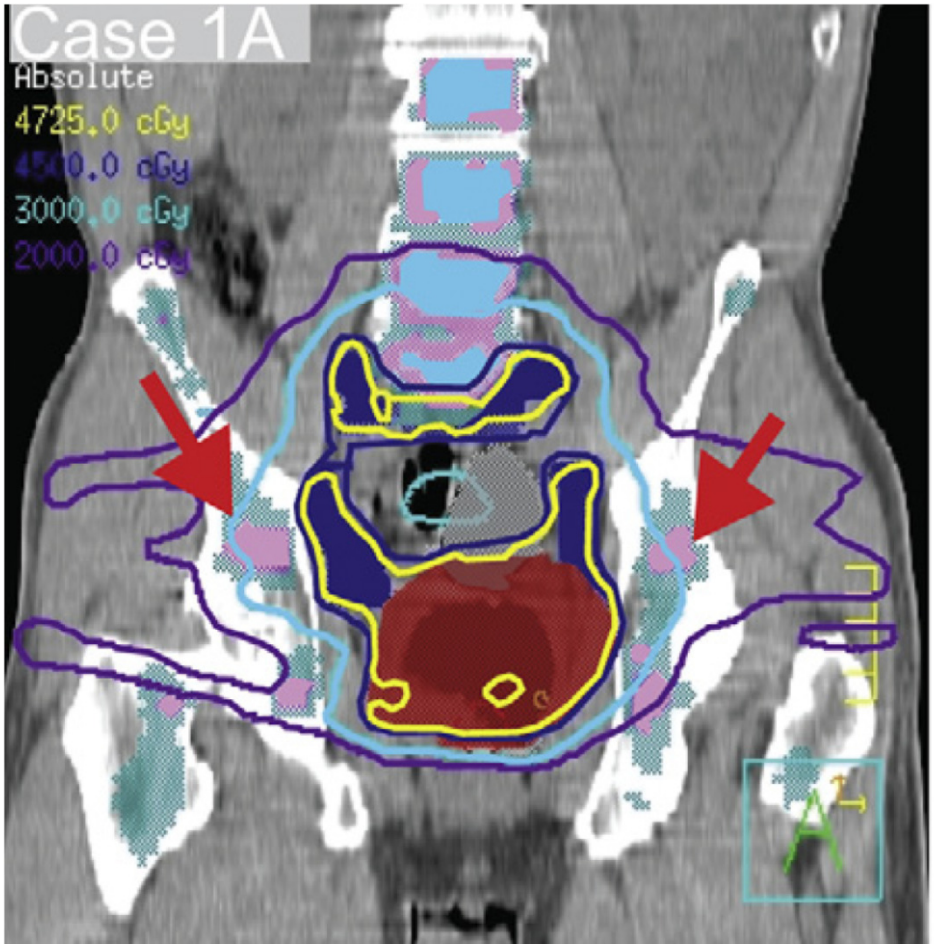
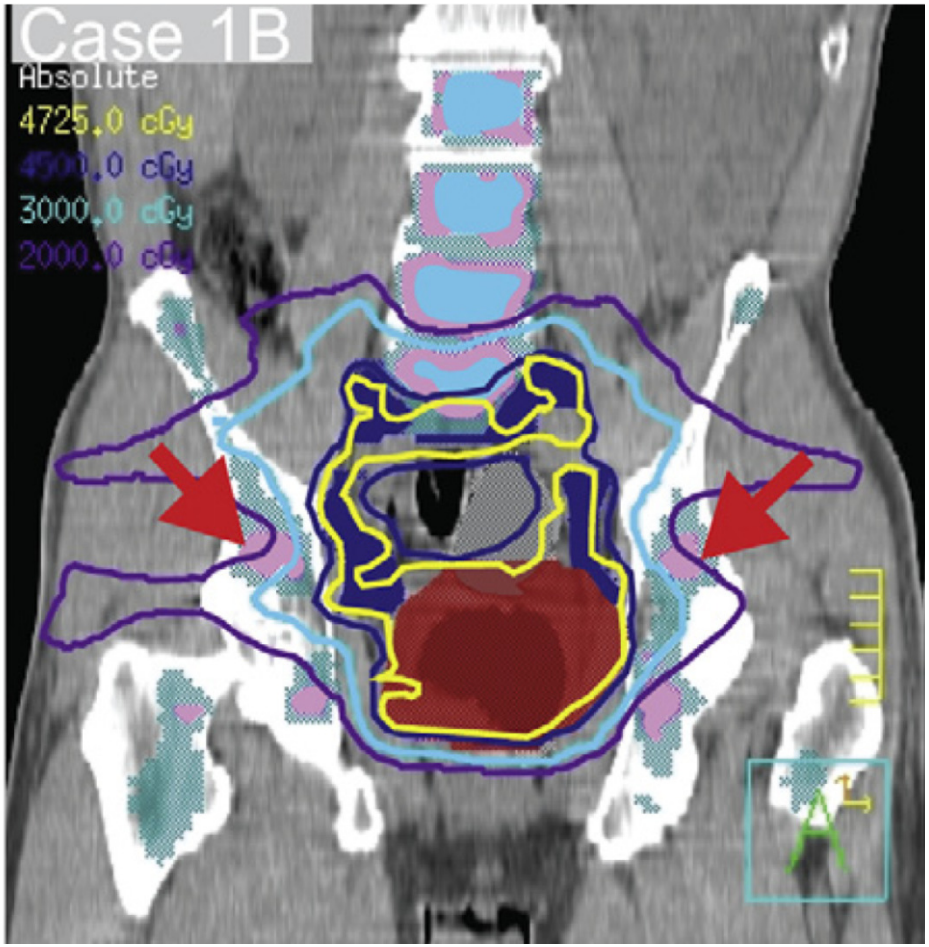


IMRT plan



IMRT-BMS

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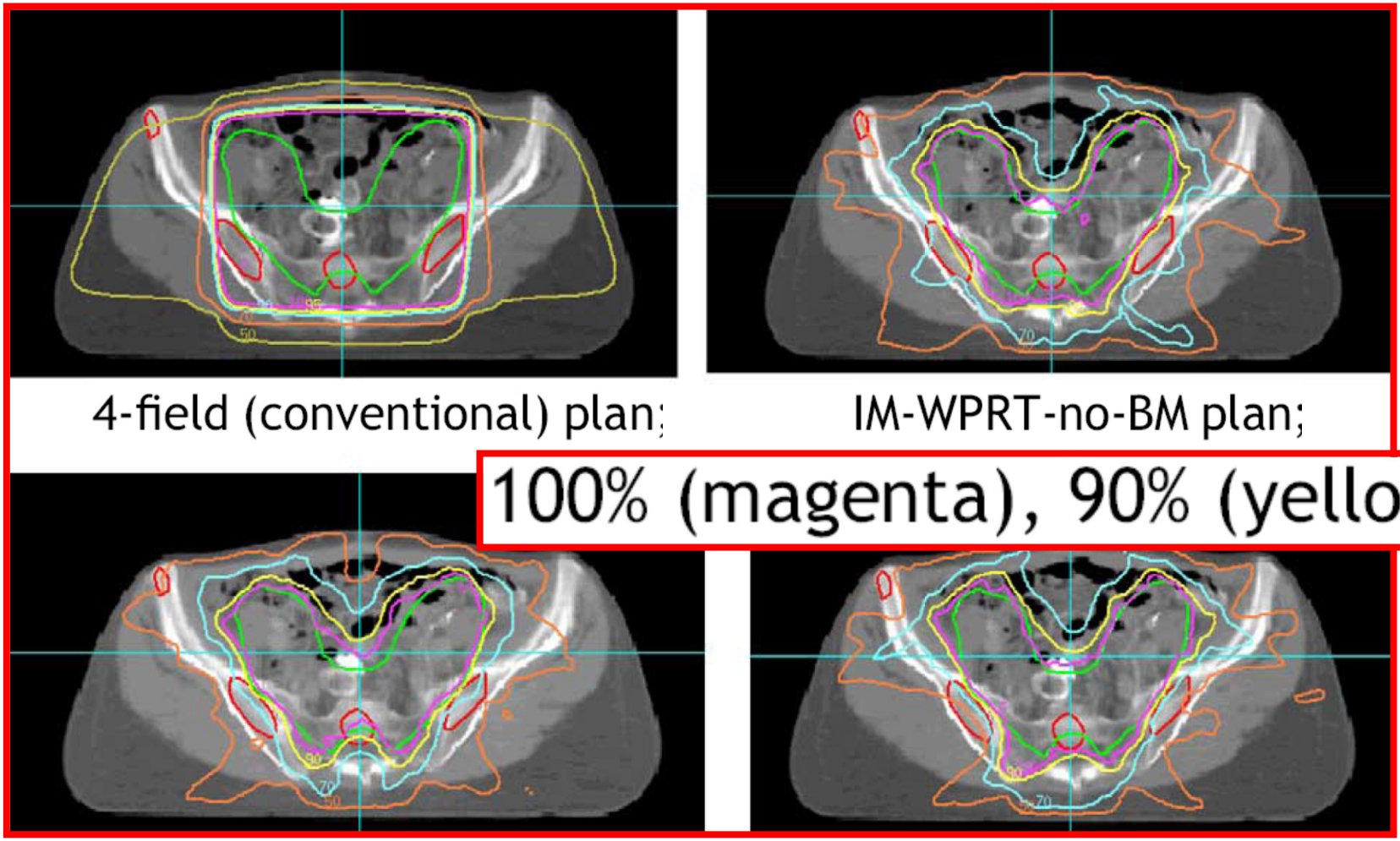

4-field (conventional) plan;

IM-WPRT-no-BM plan;

100% (magenta), 90% (yellow)

IM-WPRT-CT-BM plan

IM-WPRT-SPECT-BM plan.

Radiotherapy and Oncology 77 (2005) 11–17

DOSIMETRIC PREDICTORS OF ACUTE HEMATOLOGIC TOXICITY IN CERVICAL CANCER PATIENTS TREATED WITH CONCURRENT CISPLATIN AND INTENSITY-MODULATED PELVIC RADIOTHERAPY

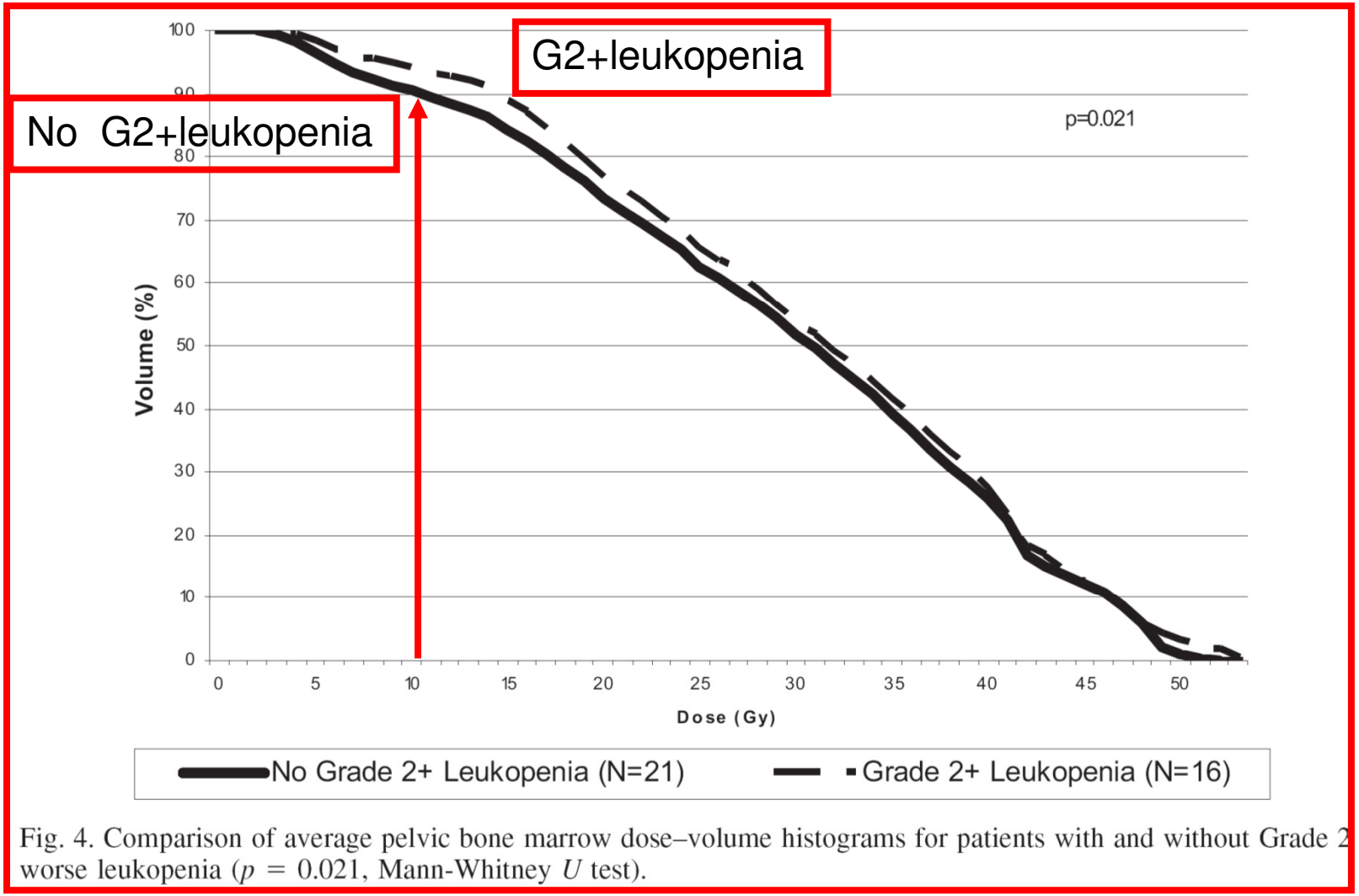

Fig. 4. Comparison of average pelvic bone marrow dose–volume histograms for patients with and without Grade 2 worse leukopenia ($p = 0.021$, Mann-Whitney U test).

Int. J. Radiation Oncology Biol. Phys., Vol. 66, No. 5, pp. 1356–1365, 2006

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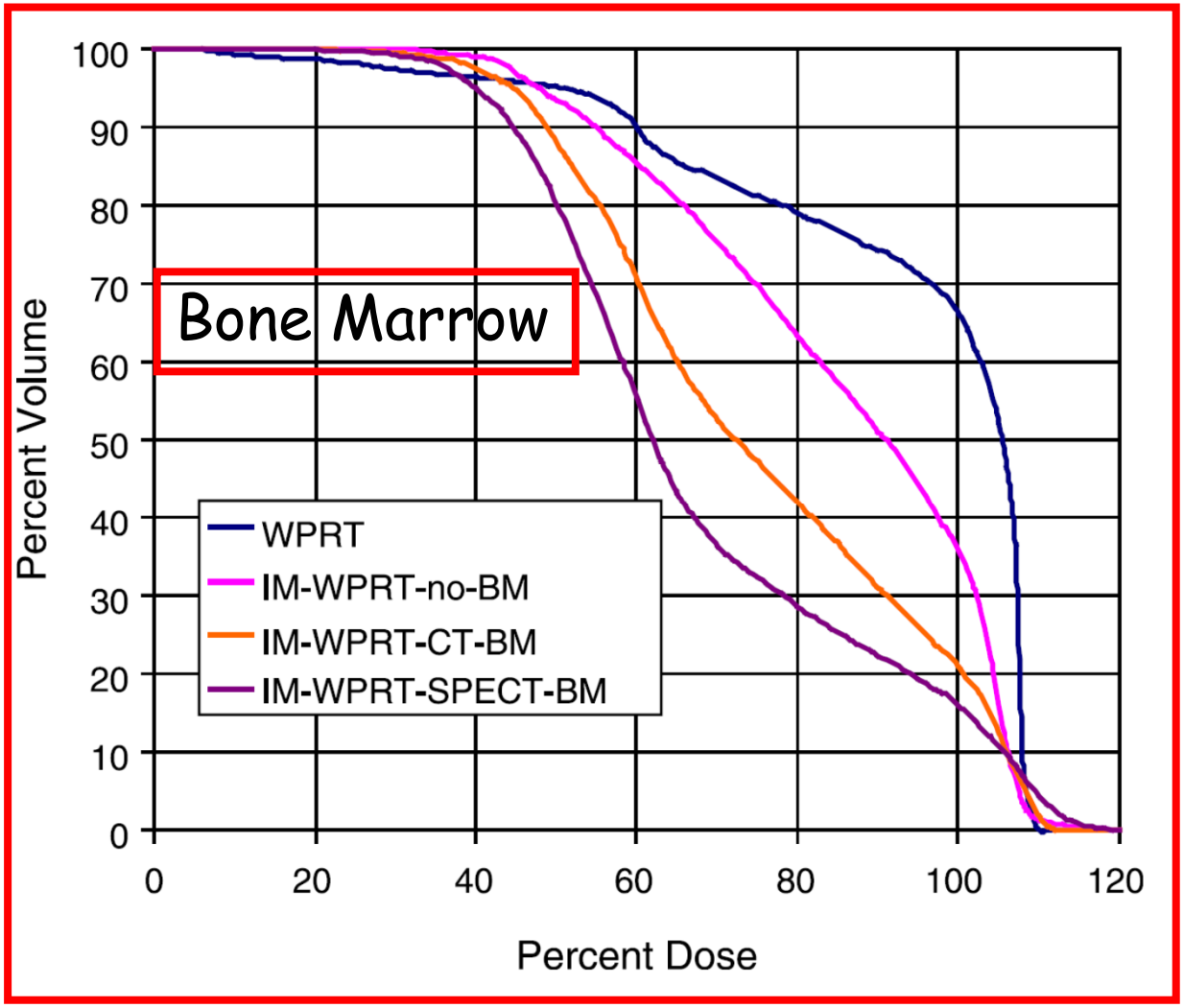

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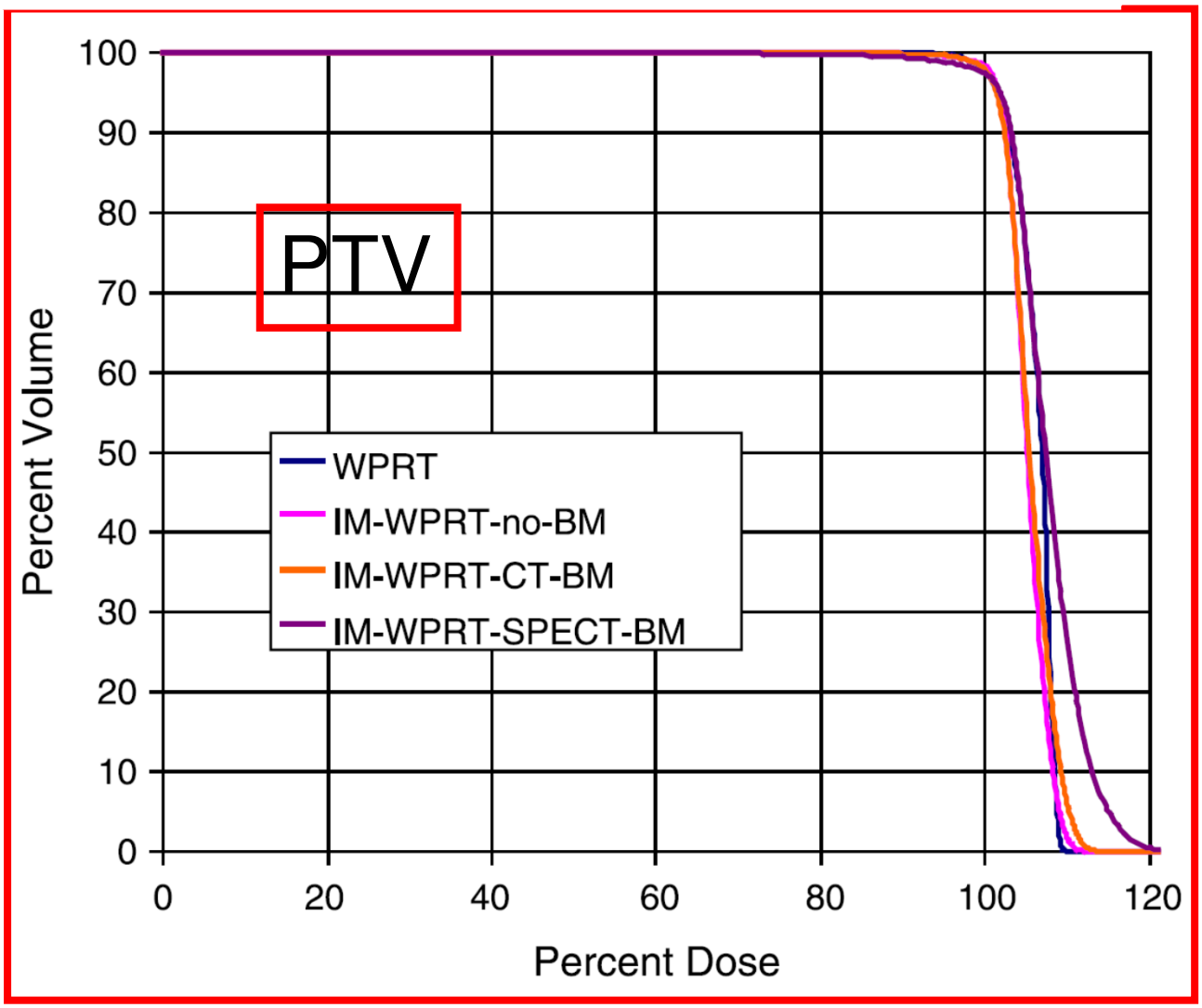
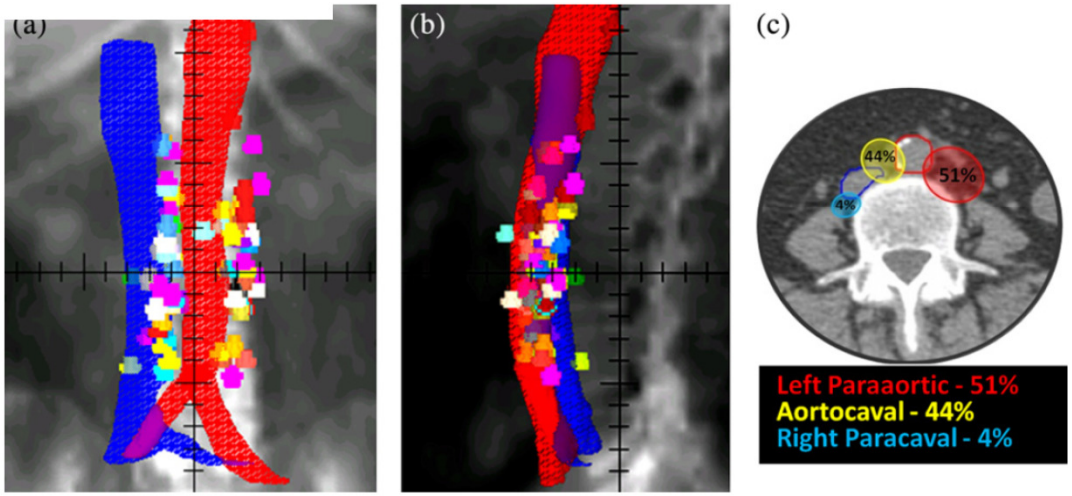


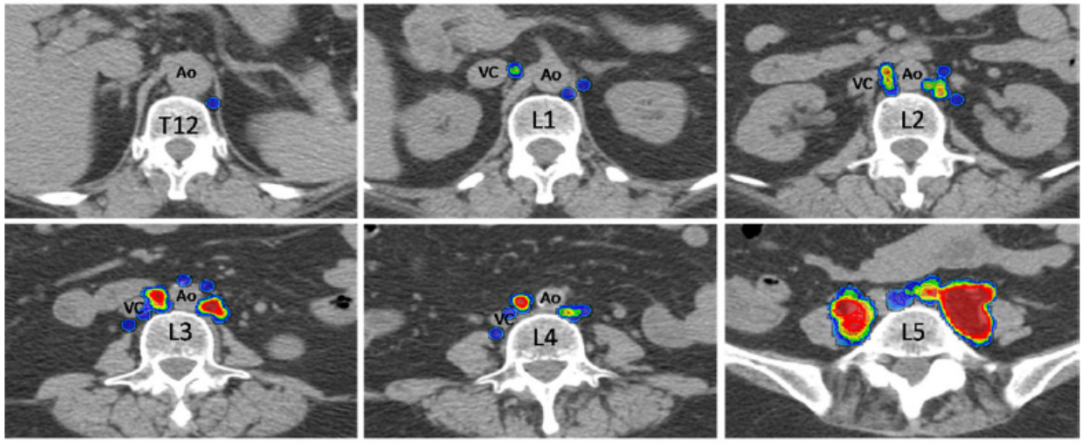
Radiotherapy and Oncology 77 (2005) 11–17

Anatomic Distribution of Fluorodeoxyglucose-Avid Para-aortic Lymph Nodes in Patients With Cervical Cancer

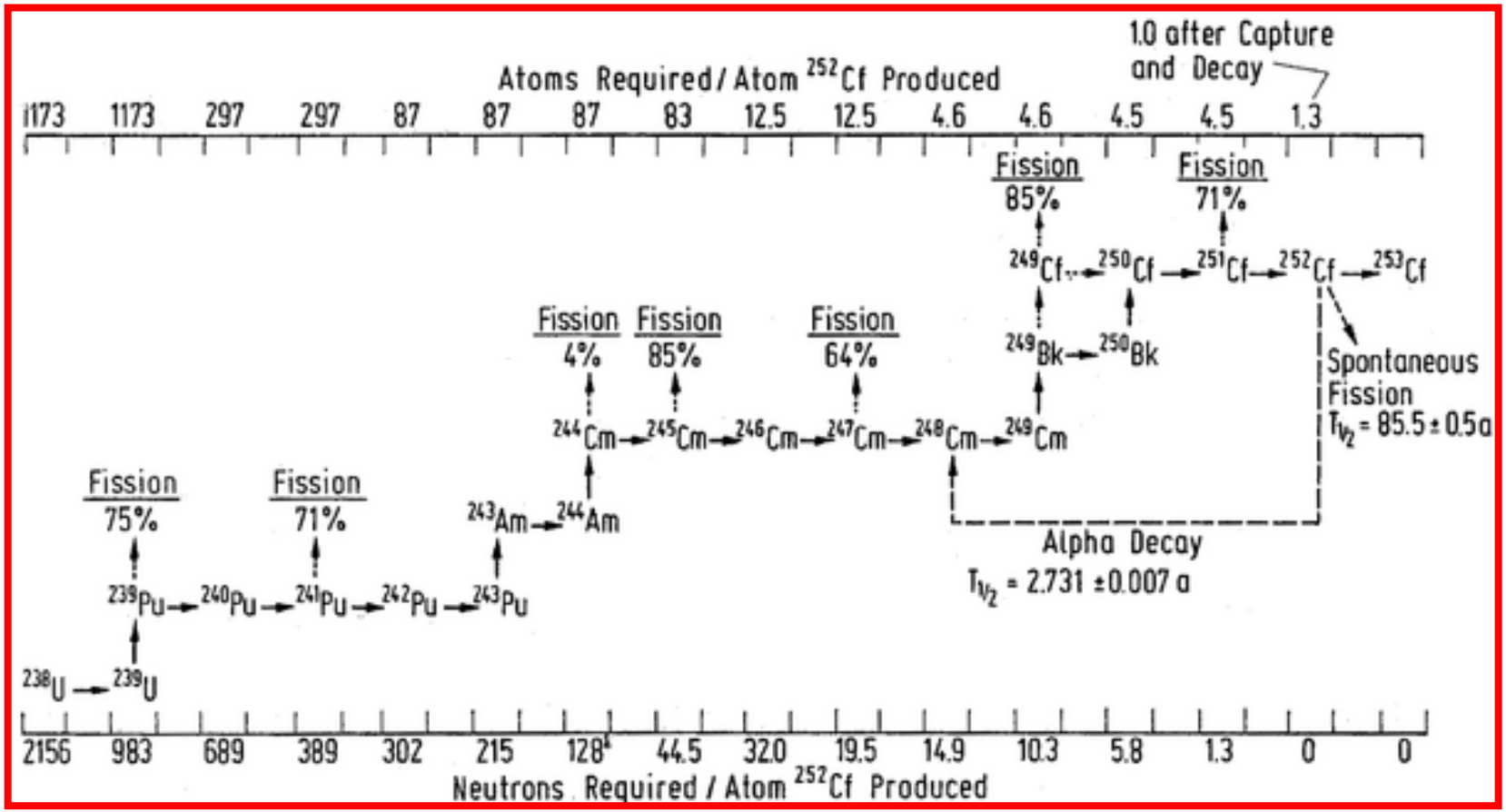
Vinita Takiar, MD, PhD,* Hiral P. Fontanilla, MD,* Patricia J. Eifel, MD,* Anuja Jhingran, MD,* Patrick Kelly, MD, PhD,* Revathy B. Iyer, MD,† Charles F. Levenback, MD,‡ Yongbin Zhang, MS,§ Lei Dong, PhD,§ and Ann Klopp, MD, PhD*

*Departments of *Radiation Oncology, †Diagnostic Radiology, ‡Gynecologic Oncology, and §Radiation Physics, The University of Texas MD Anderson Cancer Center, Houston, Texas*





A tribute to G.P. Biti: ^{252} Cf production and history of our relationship!



A tribute to G.P. Biti able to foresee ideas and solutions that I was even unable to imagine. This feature of his “BRAIN” is the astonishing characteristic, according to my poor personal opinion, of his strong personality. GRAZIE GIAMPAOLO.