BALGRIST, 06.10.2011

Radiation Therapy in extremity soft tissue sarcomas (STS)

PD Dr med Gabriela Studer
Leitende Aerztin RadioOnkologie

content

- RT goal
- Recommendations to perform RT
- Technical Aspects
- RT Volume
- RT Dose
- RT Tolerance
- RT Outcome
- Conclusions

goal

- to improve **local control**
- best possible **function** preservation
- to **avoid amputation**

recommendations

1. pre-operative RT
2. post-operative RT
3. definitive RT
4. metastases

1. pre-operative RT

- large (>5cm) deeply invading tumors
- TU close to / invading neuro-vascular bundle
- surgeons' opinion/estimation: **'wide margins ?'**

→**pre-OP statement of surgeons of high importance regarding the decision for RT**

2. post-operative RT

- tight margins / R1/2 / large tumor / grading
- rarely : boost after pre-op RT (R1/2)

3. unresected Sarcomas

Table 1. Characteristics of patients *(Continued)*

	No. of patients (%)
T Size at radiotherapy	
Range, 1–30 cm (median, 8)	
<5 cm	21 (19%)
5.5–10 cm	33 (29%)
11–20 cm	25 (22.5%)
>20 cm	8 (7%)
Undefined	25 (22.5%)
Presentation	
Primary	79 (71%)
Recurrent	33 (29%)

N=112

80%

RESULTS OF RADIATION THERAPY FOR UNRESECTED SOFT-TISSUE SARCOMAS

LUCYNA KEPKA, M.D.,* THOMAS F. DELANEY, M.D.,† HERMAN D. SUIT, M.D.,† AND SAVELI I. GOLDBERG, PH.D.‡

Int J Rad Oncol Biol Phys 2005, 852-59

3. unresected Sarcomas

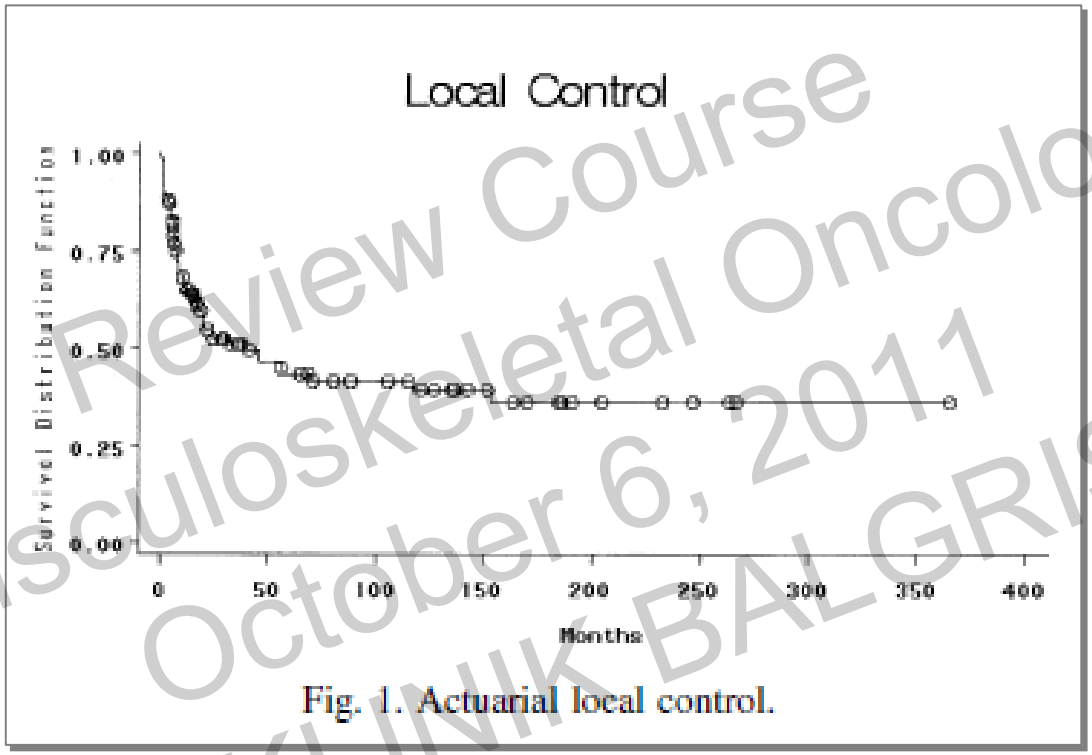

Fig. 1. Actuarial local control.

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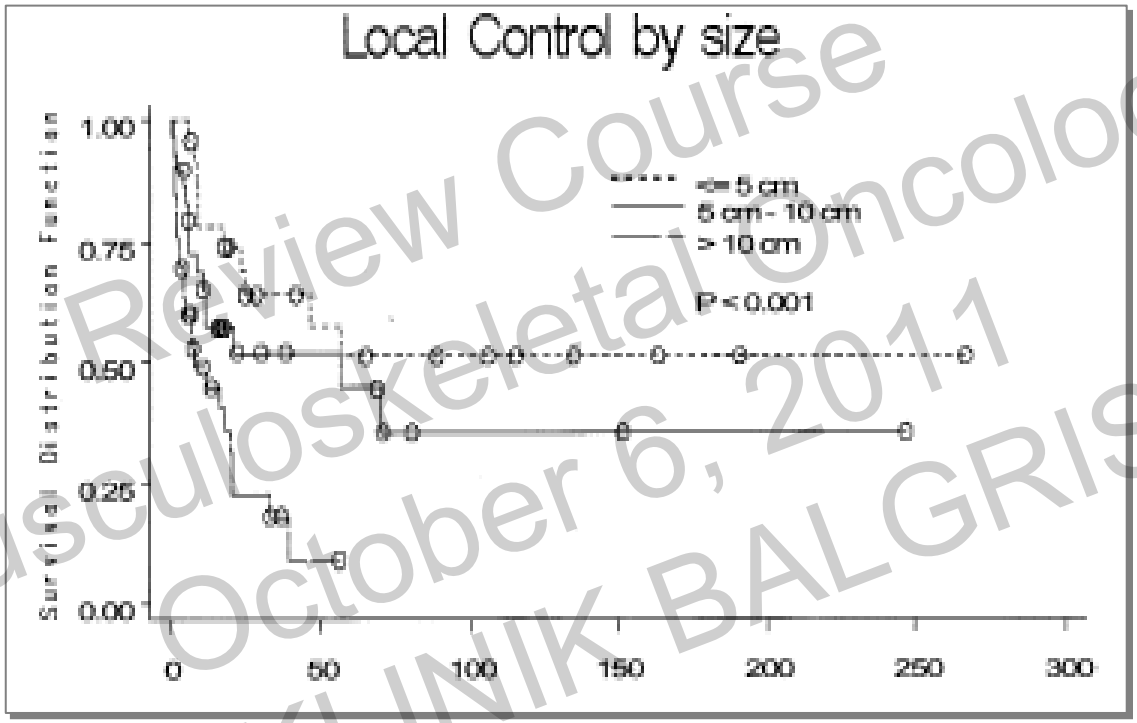

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4. Metastatic disease

- **PAIN**
- airway compression
- vascular compression
- nerval compression
- exulceration
- to avoid bone fracture
- mono-/oligo-metastatic lung mets

technical aspects

technical aspects

CBCT

sub-mm ACCURACY

INTRA-BEAM IMAGING

FFF MODE

HDMLC

GATING

technical aspects

new generations of Linearaccelerators

... are also CTs

technical aspects

Teletherapy:

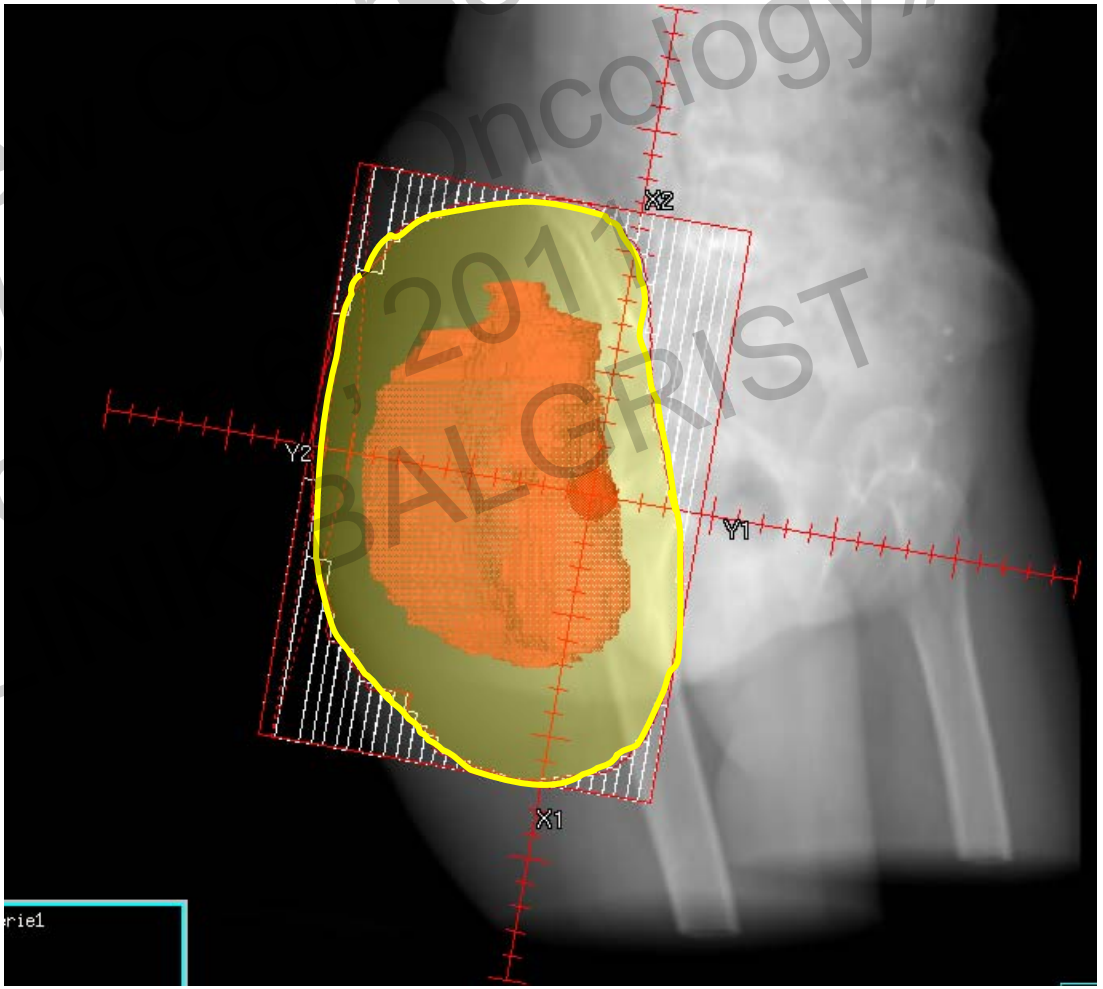
- **3DcRT**
- **IMRT / RapidArc**

(**Protons**: children/young adults!!) @ PSI

Linearaccelerator

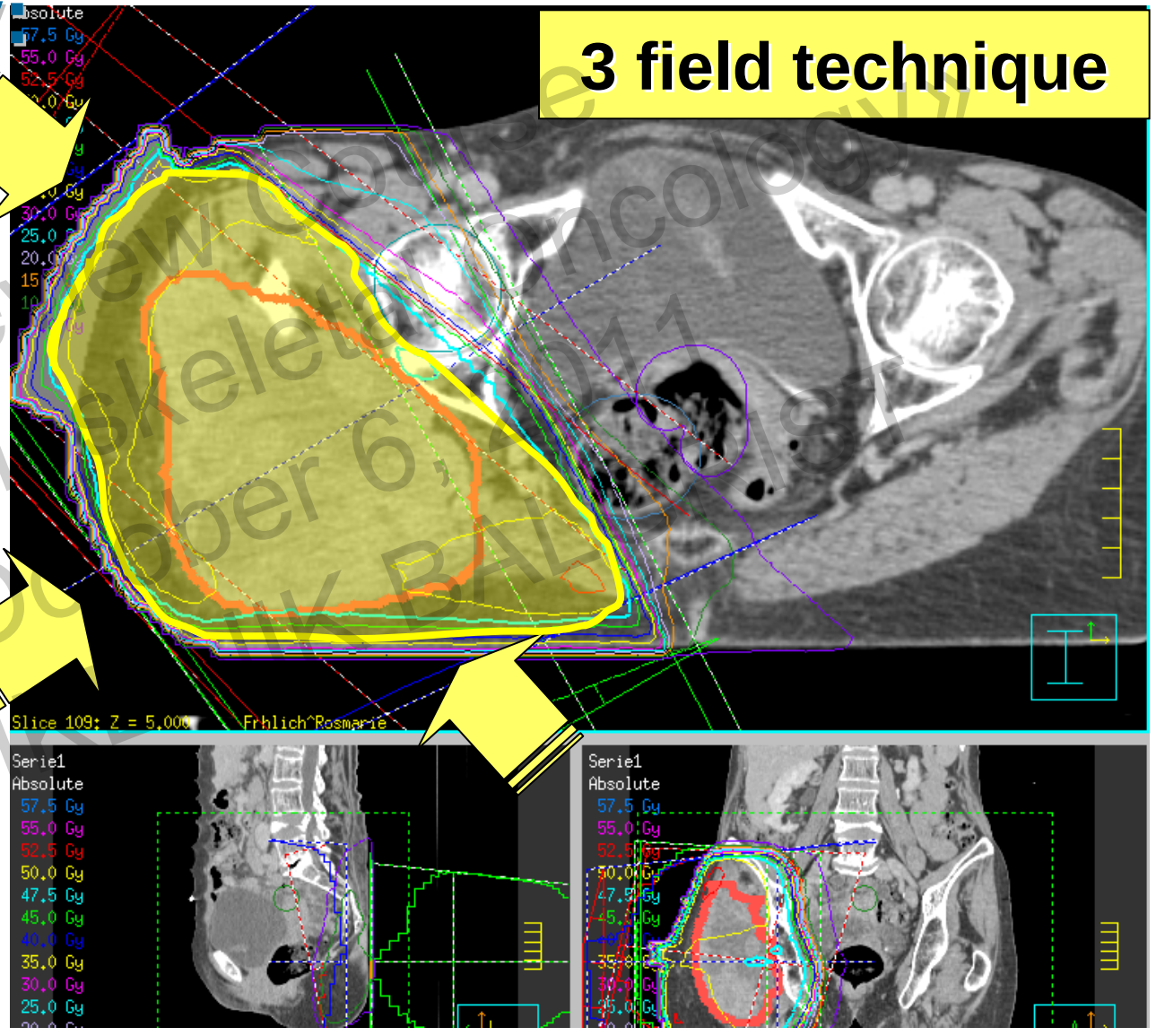
Teletherapy:

- **3DcRT**



Teletherapy:

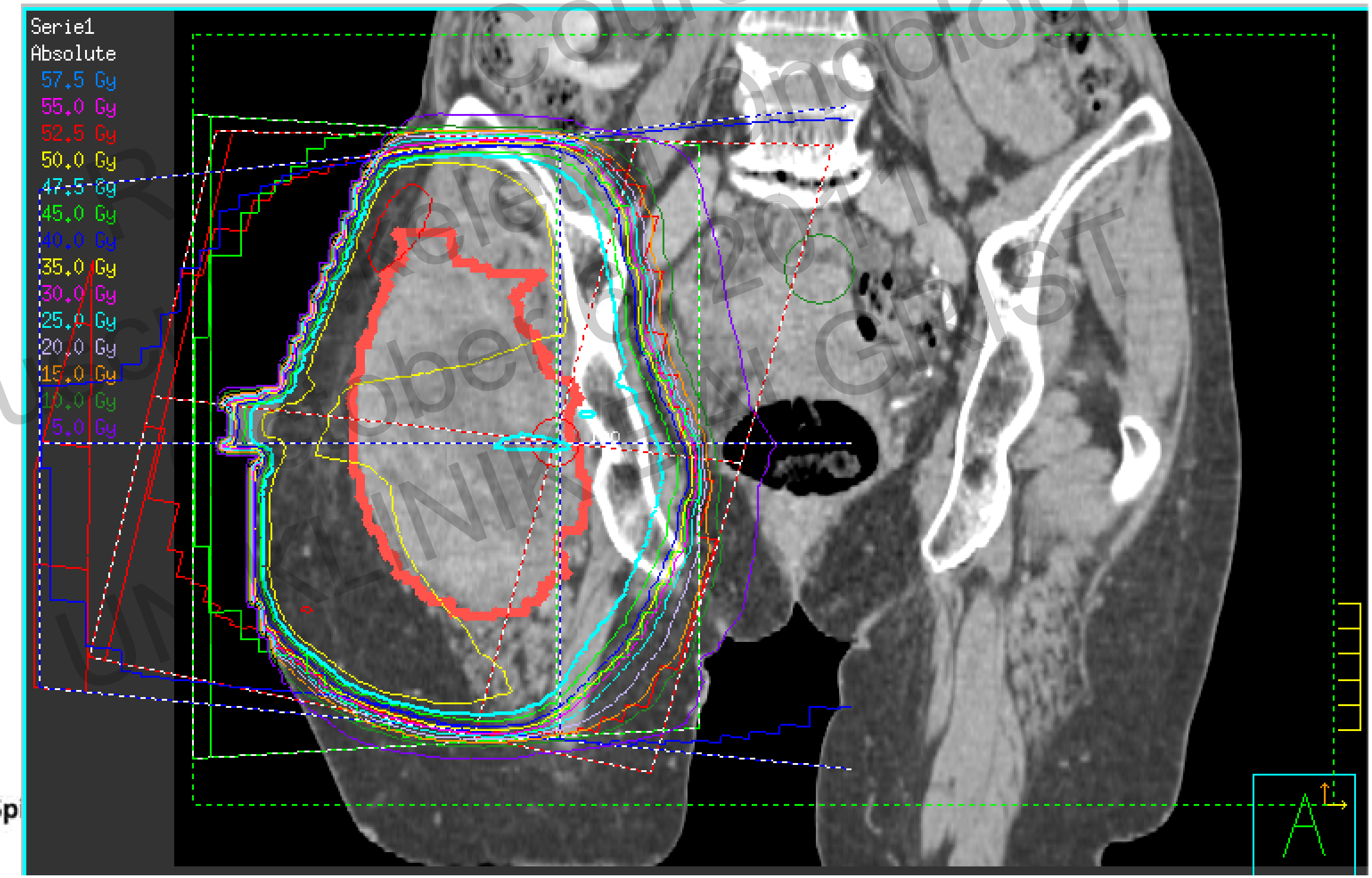
- 3DcRT



Teletherapy:

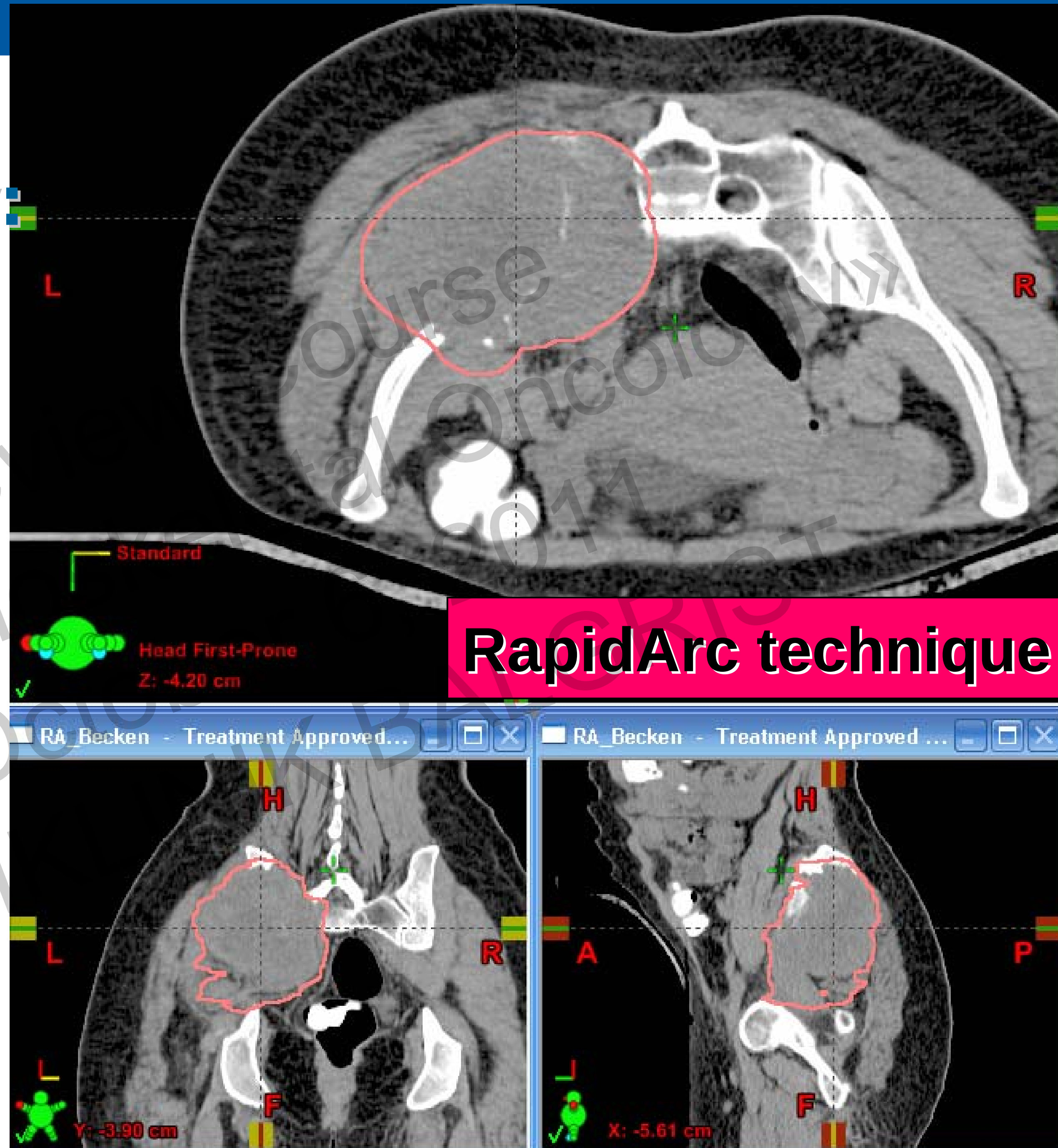
- **3DcRT**

3 field technique



Teletherapy:

- RapidArc



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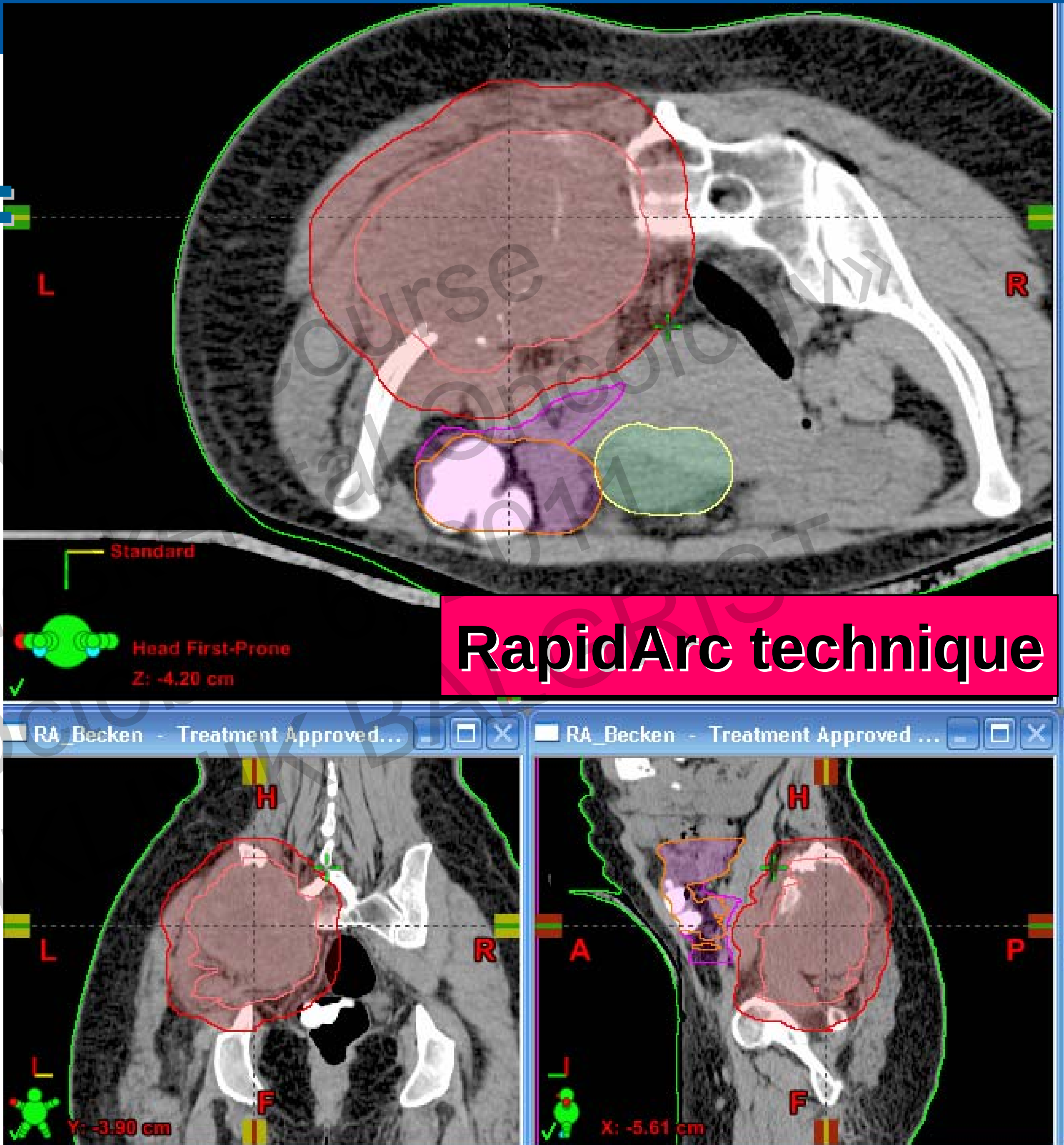
Teletherapy:

- RapidArc



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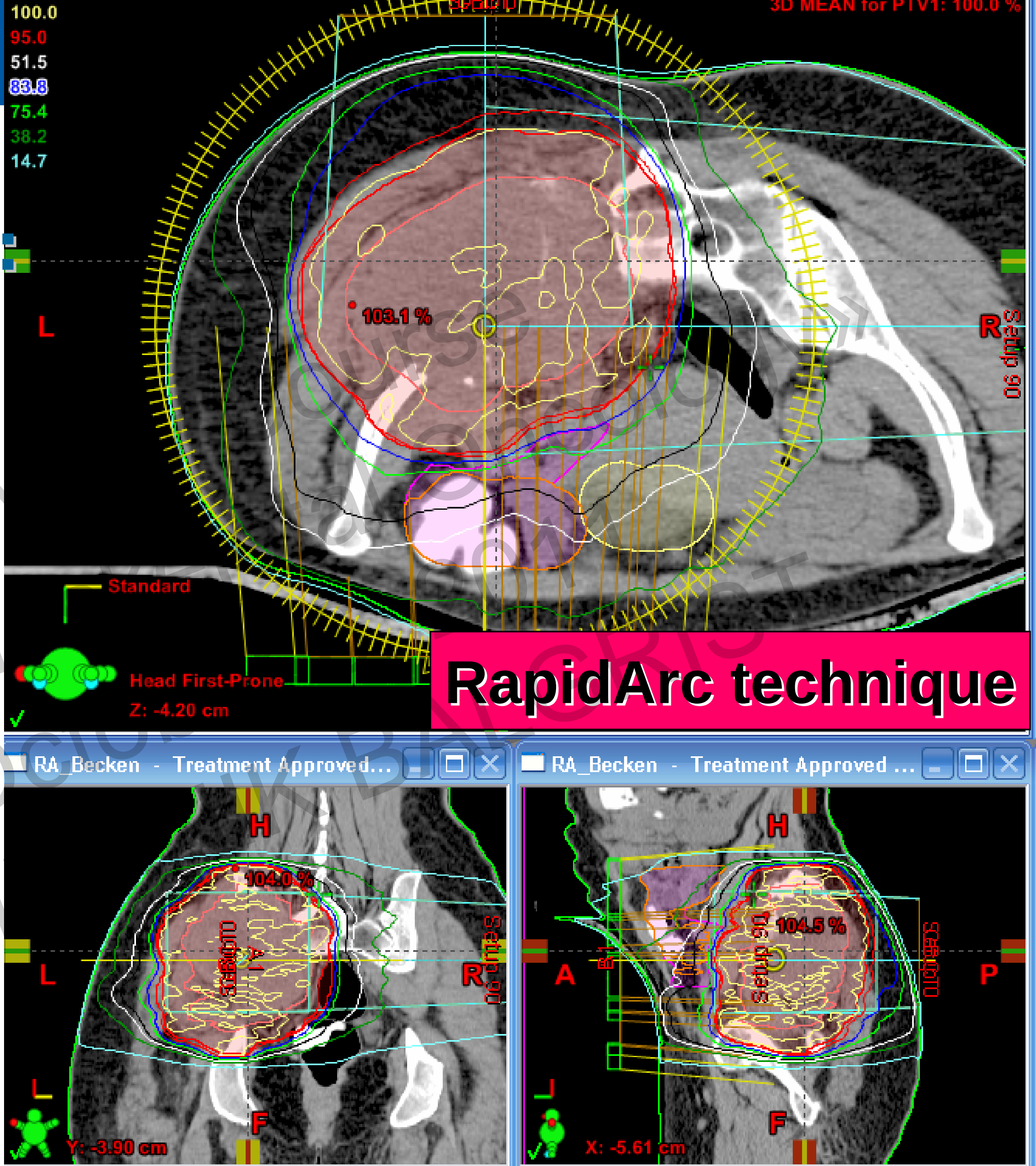
Teletherapy:

- RapidArc



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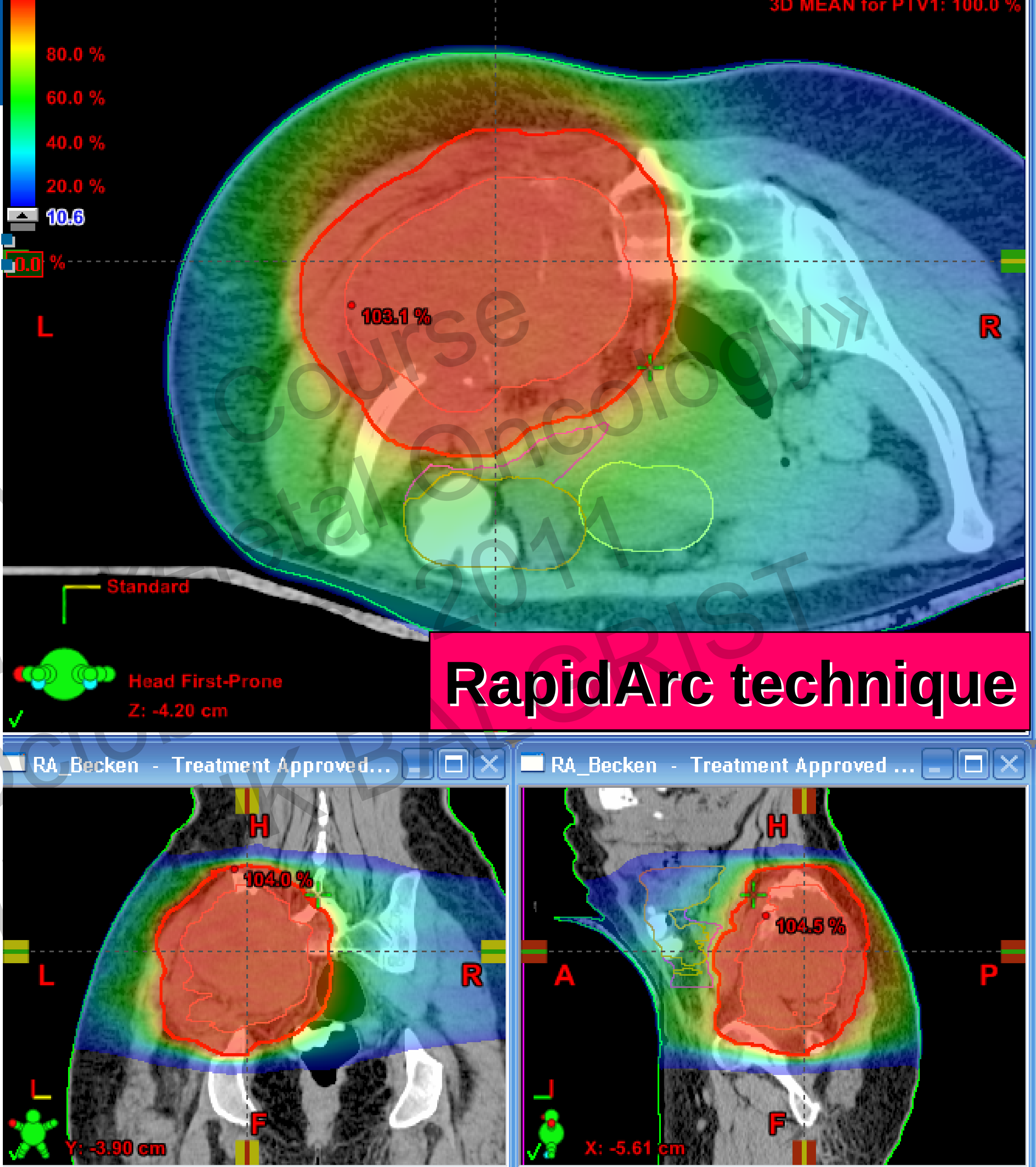

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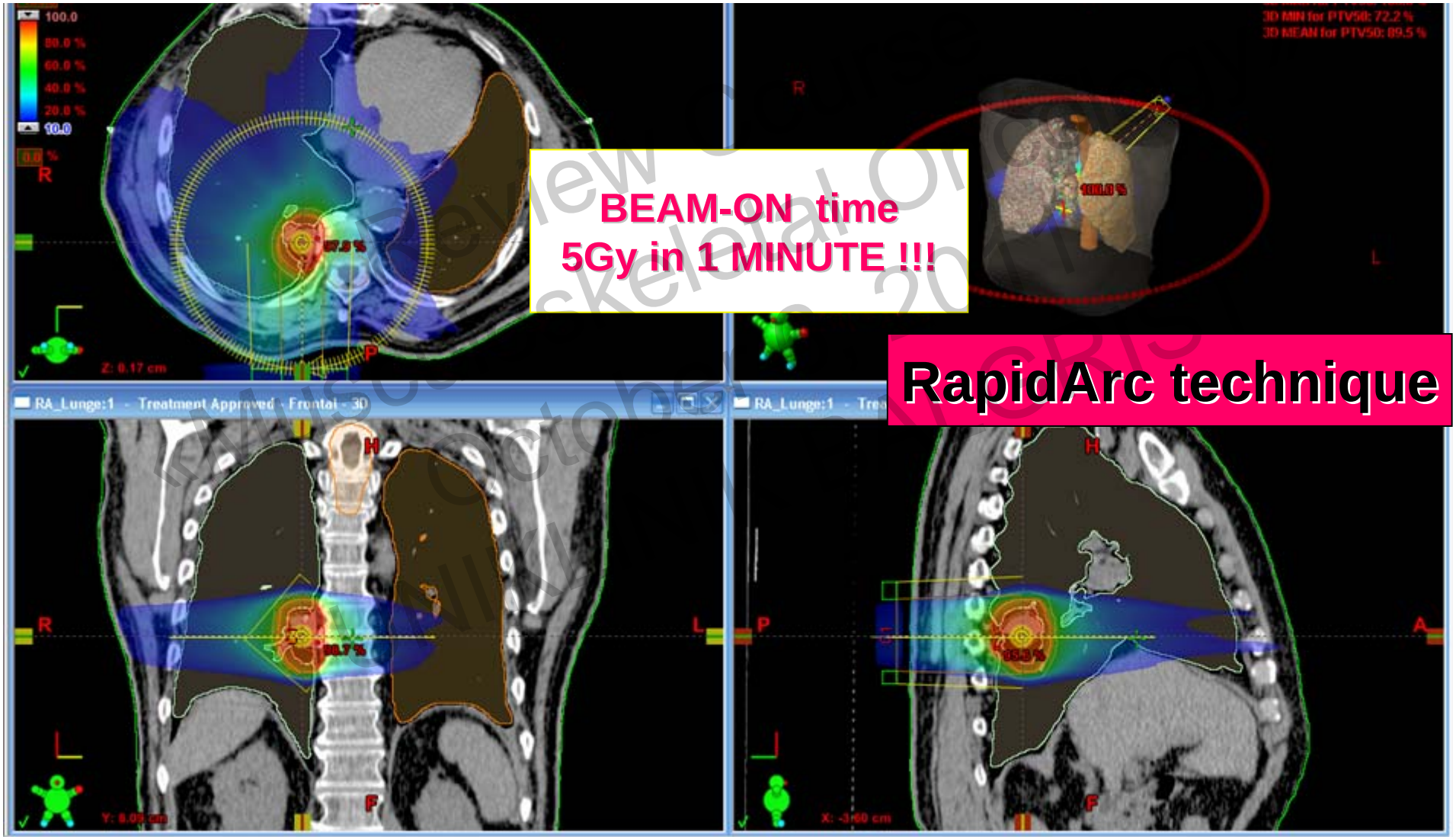
technical aspects

Highly conformal dose distribution, 6MV FFF beam,1400MU/Min
hypofractionation, high dose: 10x 5Gy (!!)



RT volume

1) lymphatic pathways rarely affected

higher risk of occult lymph node metastasis:
epithelioid sarcoma
rhabdomyosarcoma
clear cell sarcoma
extraskeletal chondrosarcoma
angiosarcoma

→LPW not to include into PTV

Lymph node metastasis in soft tissue sarcoma in an extremity.
Riad S et al. Clin Orthop Relat Res 2004;426:129–134.

2) ... the **reactive zone of edema**

surrounding the tumor,

often extending quite far from the mass,

is considered to contain microscopic disease

edema has to be included into PTV

White LM, Wunder JS, Bell RS, et al. Histologic assessment of peritumoral edema in soft tissue sarcoma. Int J Radiat Oncol Biol Phys 2005;61(5) 1439–1445.

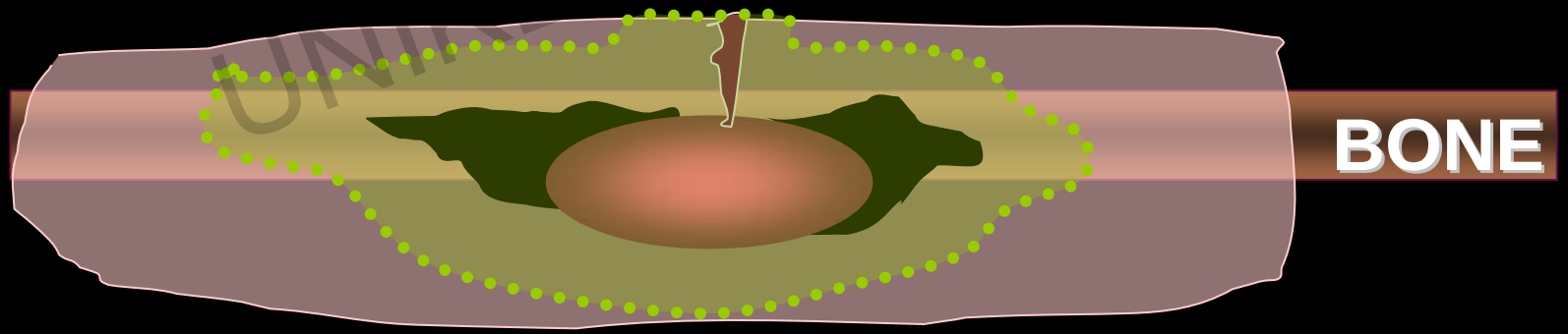
3) Tumor itself + safety margin

large margin to be included into PTV

White LM, Wunder JS, Bell RS, et al. Histologic assessment of peritumoral edema in soft tissue sarcoma. Int J Radiat Oncol Biol Phys 2005;61(5) 1439–1445.

pre-operative RT volume

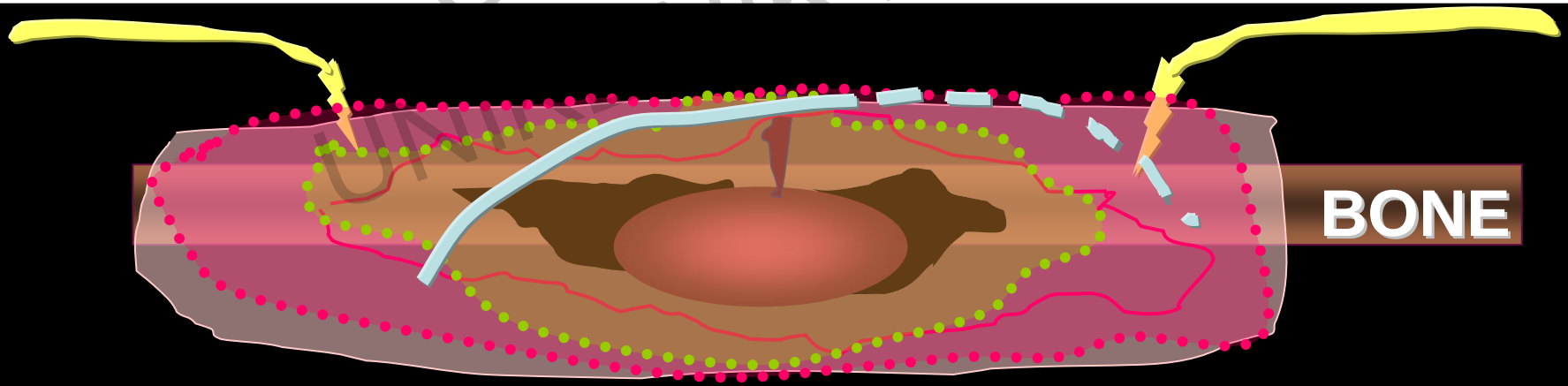
TUMOR



post-operative RT volume

TUMOR + EDEMA + biopsy canal

+ ‚lege artis' safety margins (4-5cm)= **PTV**



RT dose

pre-operative **RT (50Gy):**

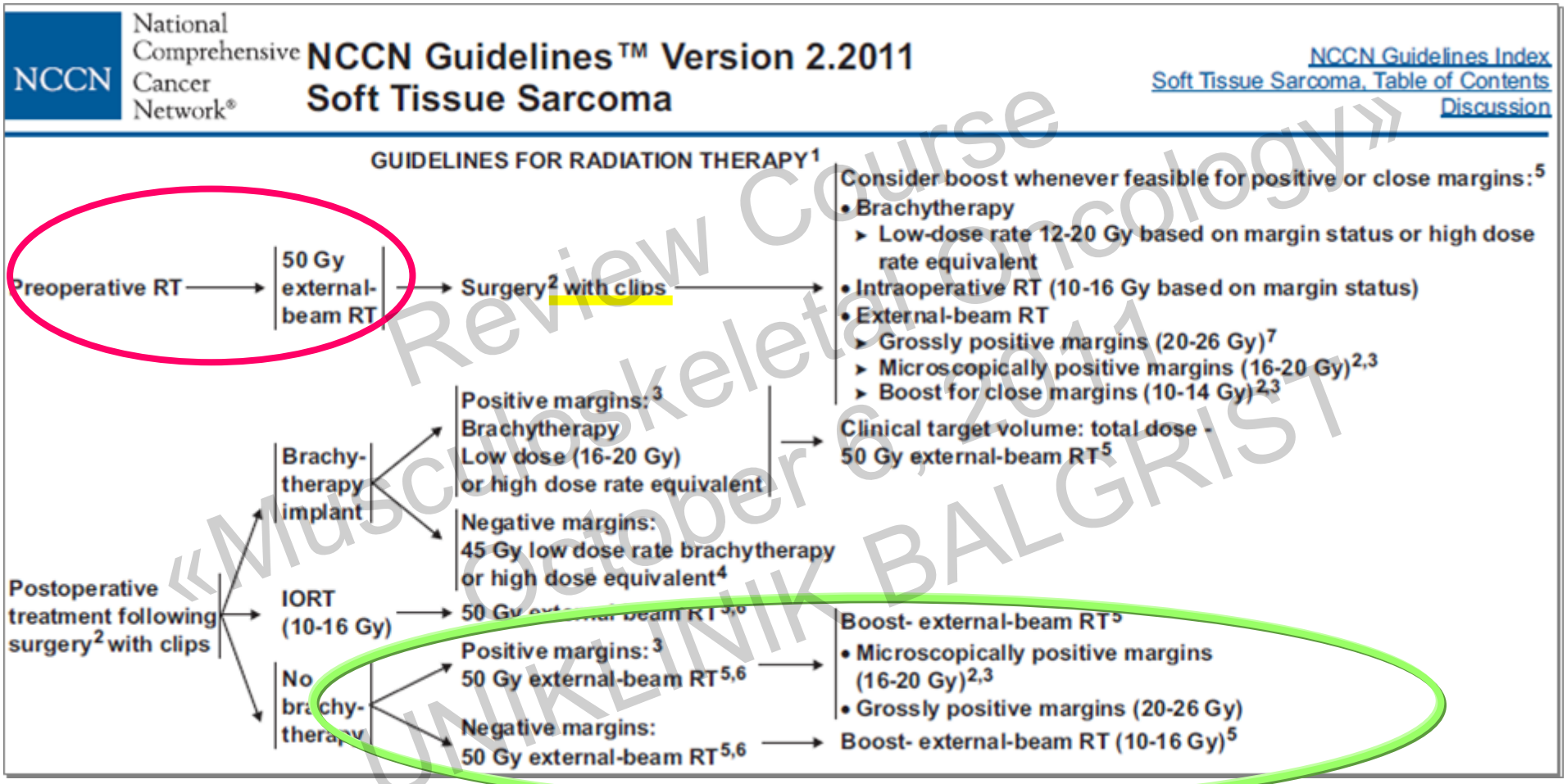
sterilization of the **environment**
sometimes shrinkage of the tumor

RT dose

post-operative **RT (66-70Gy):**

sterilization of the **environment**
sterilization of the **microscopic residuum**
sterilization of the **macroscopic residuum**

RT dose



RT dose

Radiological and pathological response following pre-operative RT

Histopathological response to treatment: 0-100%

- **low grade: median 67%**
- **high grade: median 50%**

Radiological response to treatment:

- **low grade non-myxoid: median shrinkage 14%**
- **myxoid: median shrinkage 82%**
- **high grade <1%**

→ inform the patient!

Radiother and Oncol 2010;97:404-407

Roberge D et al

RT side effects

- **f** (dose / volume / tissue / entity / individuum)
- developing **locally** (except of tiredness)

→ **long term problems starting at > ~50Gy**

RT side effects

pre-operative RT: → **well tolerated**

- early side effects: skin (f(cm2 area))
- late term effects: usually mild [fibrosis, edema, skin]

RT side effects

post-operative RT: **NOT so well tolerated**

- early side effects: **skin !!!**
- late: **edema, bone, skin, fibrosis, vessels**

RT side effects

Preoperative versus postoperative radiotherapy in soft-tissue sarcoma of the limbs: a randomised trial

	Preoperative (n=88)	Postoperative (n=94)
Wound complications*		
Yes	31 (35%)	16 (17%)
Secondary operation for wound repair	14 (45%)	5 (31%)
Invasive procedure for wound management†	5 (16%)	4 (25%)
Deep wound packing deep to dermis in area of wound at least 2 cm with or without prolonged dressings >6 weeks from wound breakdown‡	11 (35%)	7 (44%)
Readmission for wound care§	1 (3%)	0
No complications	57 (65%)	78 (83%)

*p=0·01 for yes vs no. †Without secondary operation. ‡Without secondary operation or invasive procedure. §Without secondary operation, invasive procedure, deep wound packing, or prolonged dressing.

Table 2: **Frequency of major wound complications with criteria for 182 evaluable patients**

The LANCET 2002;359(9325)
O'Sullivan B et al

RT side effects

Evidence-Based Recommendations for Local Therapy for Soft Tissue Sarcomas

Peter W.T. Pisters, Brian O'Sullivan, and Robert G. Maki

Treatment Sequencing Trade-Off Issues

Preop RT	Postop RT
Lower dose (50 Gy)	Higher dose (60-66 Gy)
Smaller field size	Larger field size
Reduced fibrosis	Increased fibrosis
Reduced edema	Increased edema
Increased wound complications (35%(?)	Wound complication risk as high as 17%

The LANCET 2002;359(9325)
O'Sullivan B et al

JCO 2007;25(8)
Pisters WT, O'Sullivan B, Maki G

disease control

→pre-op RT: better tolerance

what about disease control?

Amputation versus wide local excision +RT

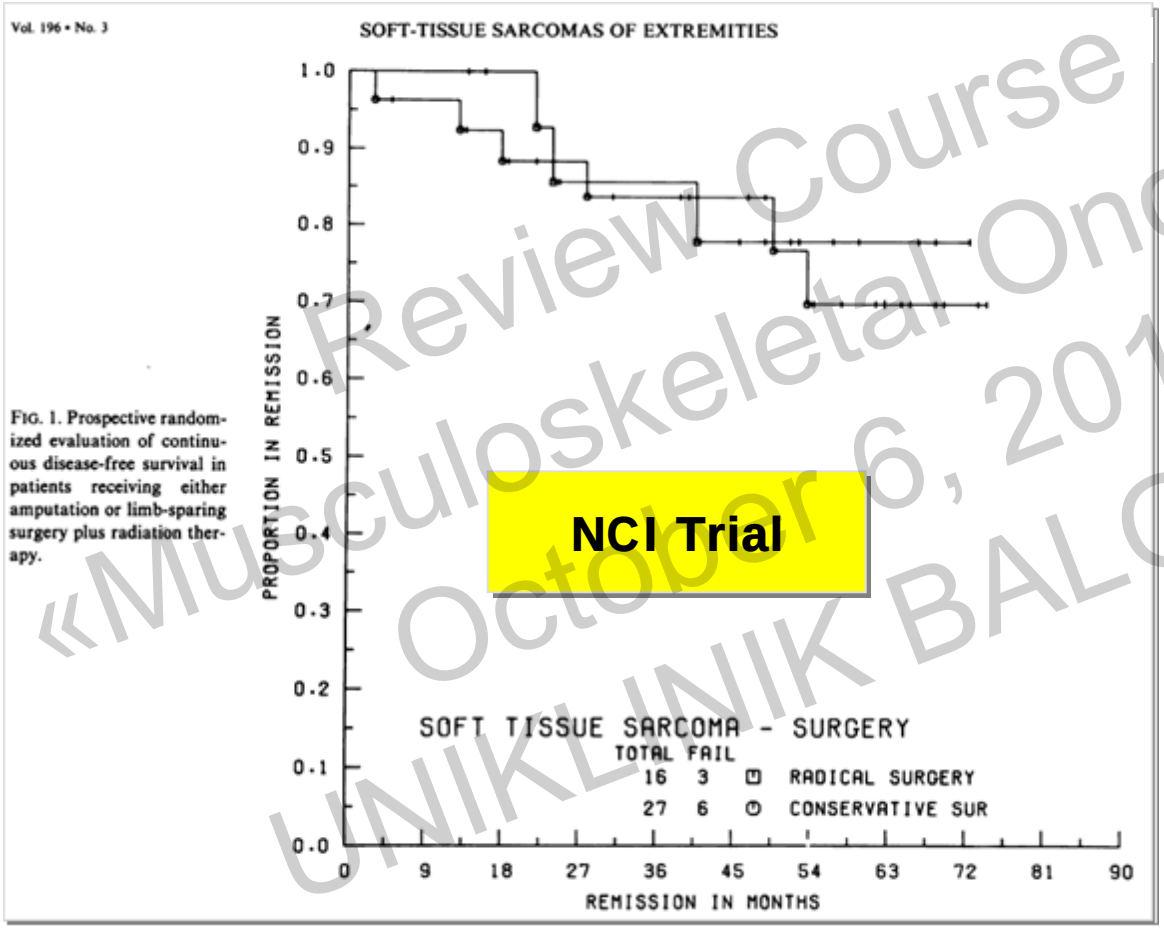
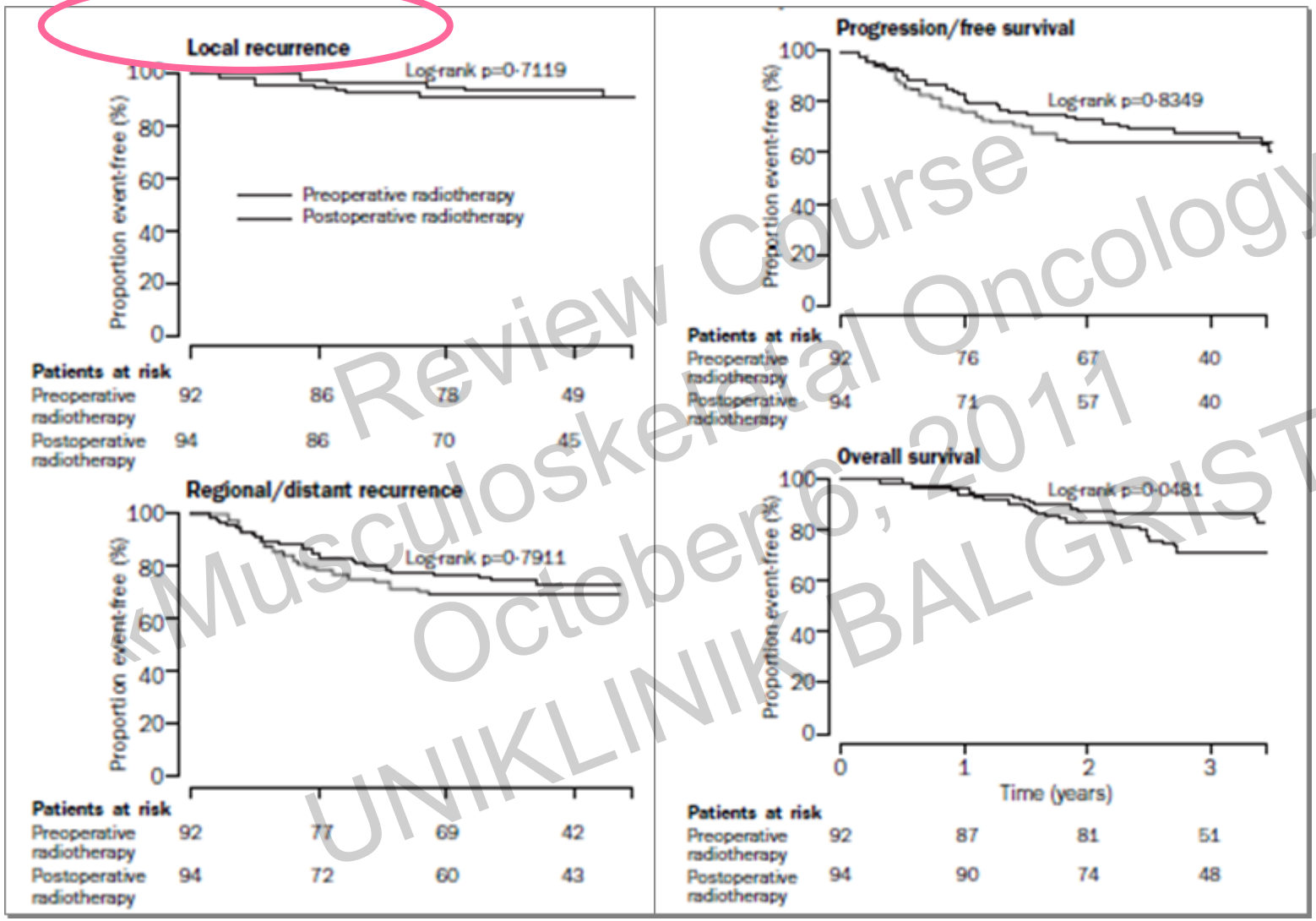


FIG. 1. Prospective randomized evaluation of continuous disease-free survival in patients receiving either amputation or limb-sparing surgery plus radiation therapy.

NCI Trial

Ann Surg **1982**;196(3):305–315
Rosenberg SA et al

disease control



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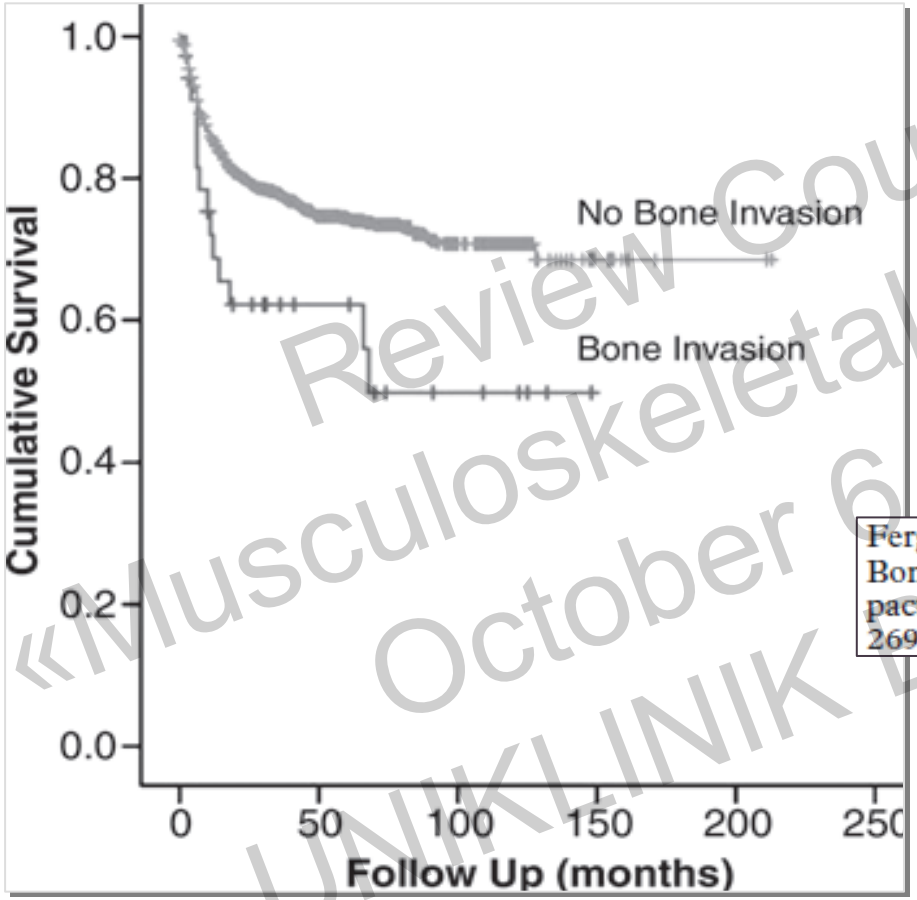
The LANCET 2002;359(9325)
O'Sullivan B et al

bone invasion



Ferguson PC, Griffin AM, O'Sullivan B, et al. Bone invasion in extremity soft-tissue sarcoma: impact on disease outcomes. Cancer 2006;106(12): 2692–2700.

Multidisciplinary Management of Soft-Tissue Sarcoma
RadioGraphics 2008;28:2069-2086

Robinson E..... and **Brian O'Sullivan**

Myxoid Liposarcoma

Radiosensitivity Translates Into Excellent Local Control in Extremity Myxoid Liposarcoma

Cancer July 15, 2009

A Comparison With Other Soft Tissue Sarcomas

Peter W. M. Chung, MB, ChB[1,6]; Benjamin M. Deheshi, MD[2,3,6]; Peter C. Ferguson, MD[2,3,6]; Jay S. Wunder, MD[2,3,6]; Anthony M. Griffin, MSc[3]; Charles N. Catton, MD[1,6]; Robert S. Bell, MD[2,3,6]; Lawrence M. White, MD[5,6]; Rita A. Kandel, MD[4,6]; and Brian O'Sullivan, MD[1,6]

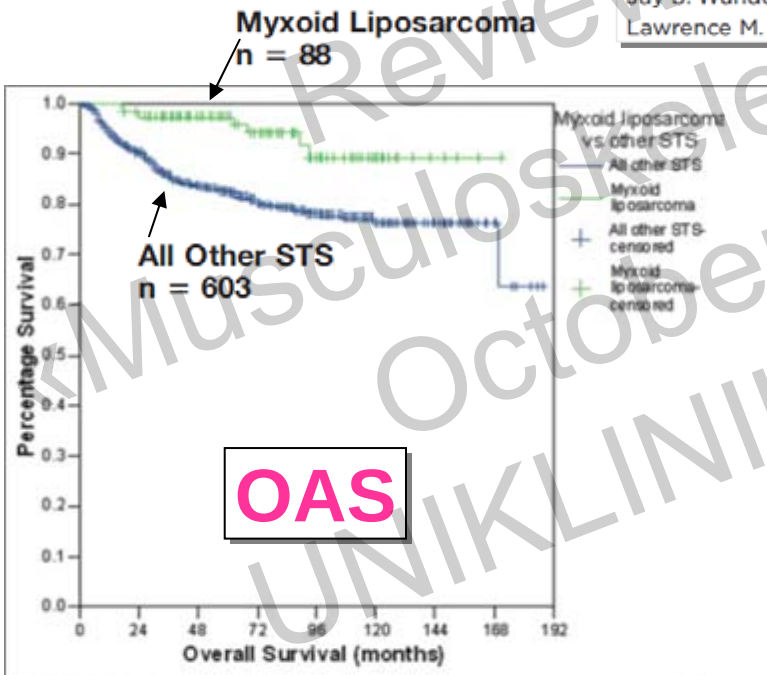


FIGURE 1. Overall survival myxoid liposarcoma versus other STS subtypes ($P = .0008$).

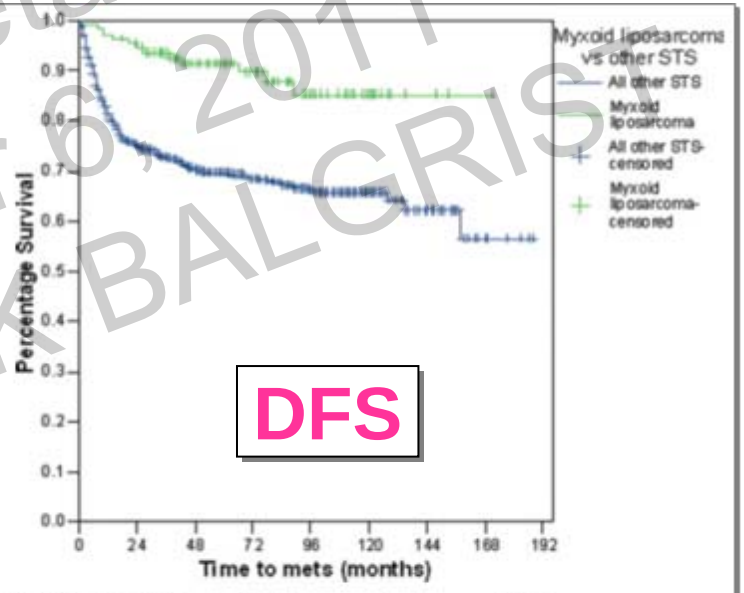


FIGURE 2. Metastasis-free survival myxoid liposarcoma versus other STS subtypes ($P = .0001$).

disease control

Grade I STS

(no differenciation between well differentiated liposarcoma (and=G1) and G1 myxoid liposarcoma)

Randomized prospective study: Benefit of adjuvant RT (n:141)

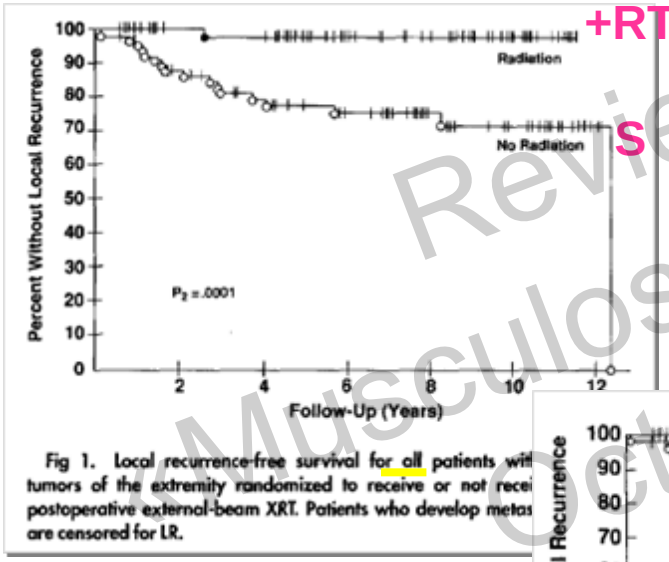


Fig 1. Local recurrence-free survival for all patients with tumors of the extremity randomized to receive or not receive postoperative external-beam XRT. Patients who develop metastases are censored for LR.

LC

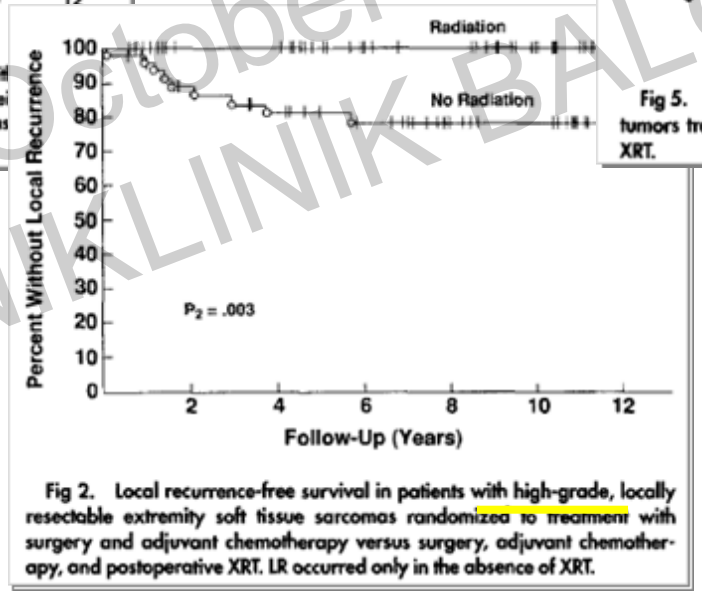


Fig 2. Local recurrence-free survival in patients with high-grade, locally resectable extremity soft tissue sarcomas randomized to treatment with surgery and adjuvant chemotherapy versus surgery, adjuvant chemotherapy, and postoperative XRT. LR occurred only in the absence of XRT.

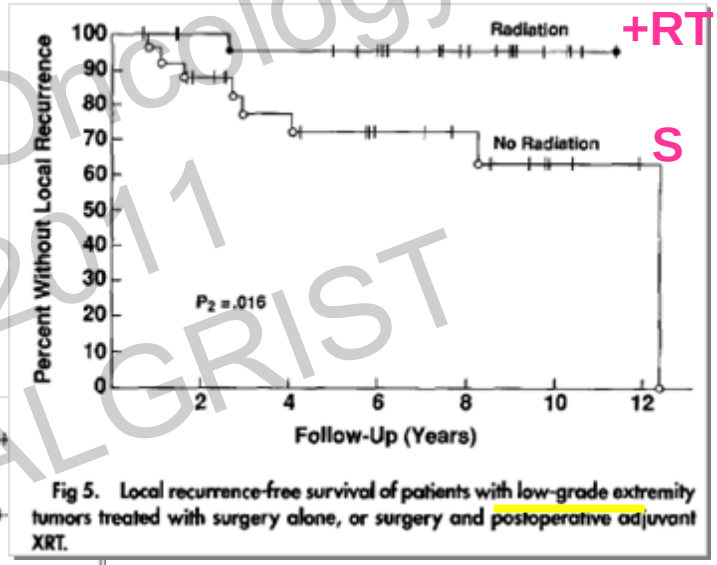


Fig 5. Local recurrence-free survival of patients with low-grade extremity tumors treated with surgery alone, or surgery and postoperative adjuvant XRT.

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(NCI) Arch Surg 1993;128:1336-43

Marcus SG et al

JCO 1998;16:197-203

Yang JC et al

MULTIDISCIPLINARY APPROACH

-pre-treatment discussion of procedure
-individual, argument-based solutions
-tight interdisciplinary cooperation
-Q: f(experience, interdisciplinary approach, EBM)
-QA: f(FU/evaluation of results)

PRE-OPERATIVE RT favoured

- RT tolerance better due to less dose + smaller volume
- same disease control