Personalizing Local Treatment of Soft Tissue Sarcoma

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Through the 1950s standard personalized therapy for STS was amputation two joints above the lesion

This was also the time when new, non-surgical approaches were launched

A Critical Review of the Management of Soft-Tissue Sarcomas

R. LEE CLARK, JR., M.D.,

RICHARD G. MARTIN, M.D.,

AND

E. C. WHITE, M.D.

Reprinted from THE JOURNAL-LANCET, Minneapolis, July 1959, Vol. 79, No. 7

The first published use of chemotherapy in STS?

CHEMOTHERAPEUTIC AGENTS USED IN TREATMENT OF PATIENTS WITH SOFT TISSUE SARCOMAS

Agents	Anatomic Site	Histologic diagnosis	Number of cases	Dosage and Route of administration	Results
ALKALATING:					
Nitromin	Extremities	Fibrosarcoma, Unclassified,	4	I.V., 350 to 1,500 mg. over 30-day period	Negative to minimal regression in all but 2 patients. The first with fibrosarcoma of trunk had marked regression with 175 mg. of PAM I.V. in divided doses. The second patient with lymphangiosarcoma following radical mastectomy had clinically complete regression after perfusion with 50 mg. of PAM and 10 mg. of HN2. Two foci found in amputated arm.
Nitrogen mustard	Trunk Buttock	Liposarcoma, Angiosarcoma, Synovial sarcoma,	7	Perfusion, 10 to 50 mg. I.V., 10 to 20 mg.	
Phenylalanine mustard	Head	Lymphangio-sarcoma, Postrad. mastectomy,	7	Orally, 20 mg. Perfusion, 50 to 100 mg. I.V., 20 to 50 mg.	
ThioTepa		Rhabdomyo-sarcoma	1	Injected into tumor 8 mg. × 2	
ANTIMETABOLITE:					
Amethopterin	Head	Rhabdomyo-sarcoma,	1	I.V., 2.5 mg. × 8	No objective regression
	Buttock	Angiosarcoma	1	I.V., 2.5 mg. × 14	
ANTIBIOTIC:					
Actinomycin-D	Trunk Extremity	Fibrosarcoma, Angiosarcoma,	5	I.V. in divided doses totaling 250 to 5,500 gamma	Temporary regression in case of rhabdomyosarcoma given Actinomycin-D. 950 gamma given I.V. prophylactically to 16-month-old child after radical wide excision of lesion of arm.
Carzinophilin	Head Buttock	Rhabdomyo-sarcoma	2	105,000 units total dose I.V. over 3-wk. period	
STEROID:					
Cortisone				15 mg. every 5 hours × 5	Used in some cases with HN2 in an attempt to potentiate the action of HN2. Unable to evaluate.
Combination of above agents		In several cases, more than one agent has been tried.			No added benefit

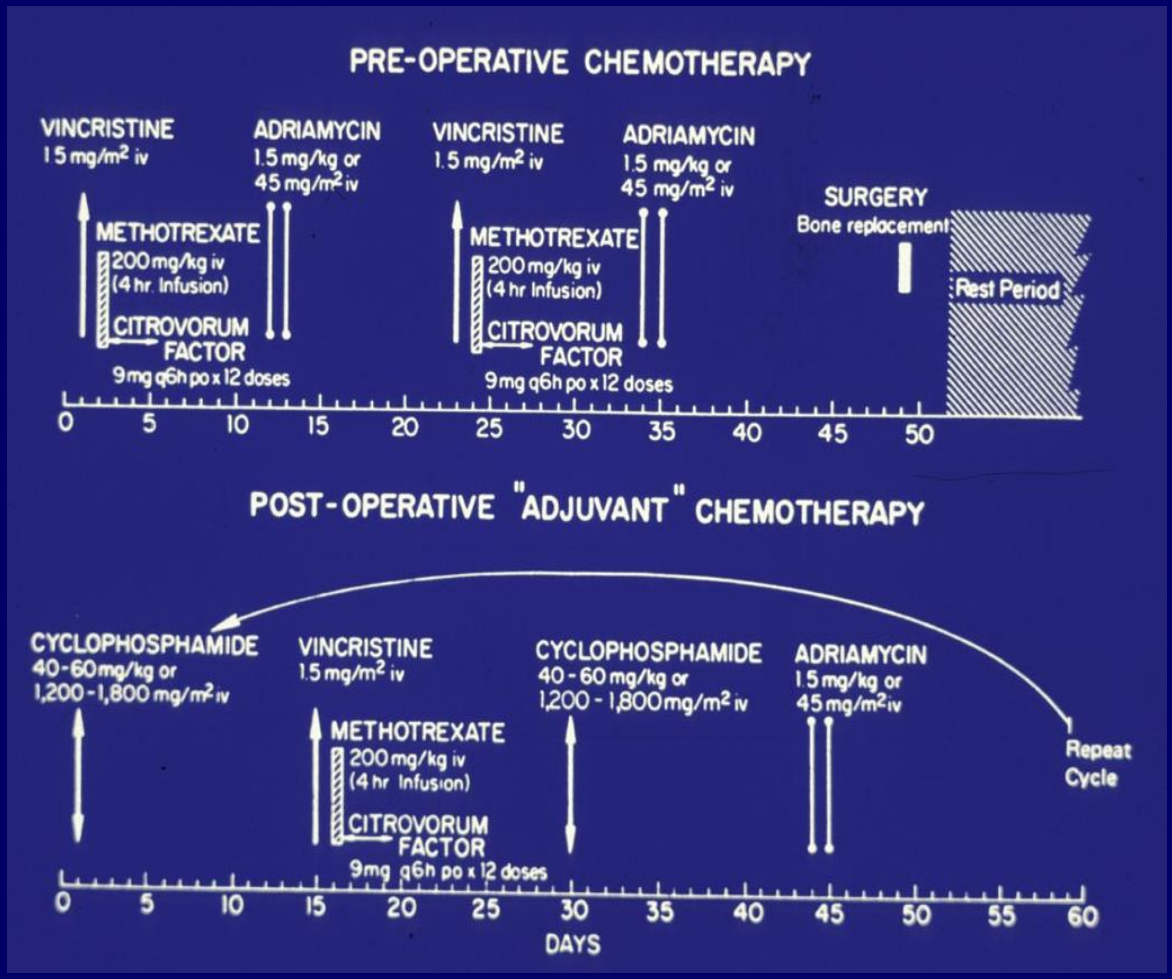
Neoadjuvant chemotherapy began as an extension of primary local therapy

CHEMOTHERAPY, *EN BLOC* RESECTION, AND PROSTHETIC BONE REPLACEMENT IN THE TREATMENT OF OSTEOGENIC SARCOMA

GERALD ROSEN, MD,* M. LOIS MURPHY, MD,† ANDREW G. HUVOS, MD,‡ MANUEL GUTIERREZ, MD,‡ AND RALPH C. MARCOVE, MD**

Cancer 37:1–11, 1976.

Neoadjuvant chemotherapy began as an extension of primary local therapy



From pediatric bone we extrapolated to adult soft tissue…

Neoadjuvant chemotherapy as an extension of primary local therapy

Reprinted from: ANNALS OF SURGERY, Vol. 211, No. 4, April 1990

Preoperative Chemotherapy for Soft-tissue Sarcomas of the Extremities

CHRISTOPHER M. PEZZI, M.D., RAPHAEL E. POLLOCK, M.D., HARRY L. EVANS, M.D., JAMES G. LORIGAN, M.D., THOMAS A. PEZZI, B.S., ROBERT S. BENJAMIN, M.D., and MARVIN M. ROMSDAHL, M.D., PH.D.

From the Departments of Surgery, Pathology, Radiology, and Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, Texas

Neoadjuvant chemotherapy as an extension of primary local therapy

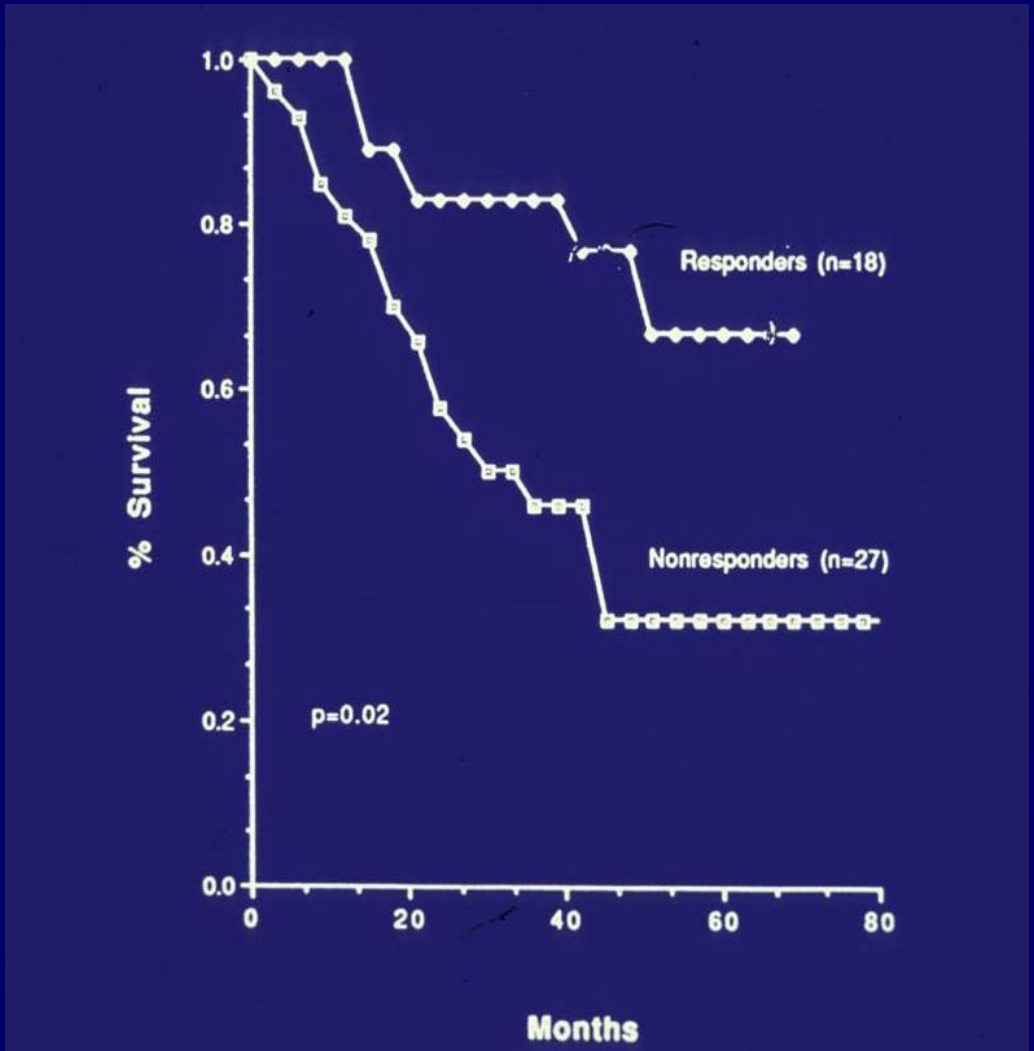


FIG. 4. Overall survival based on clinical response to preoperative chemotherapy.

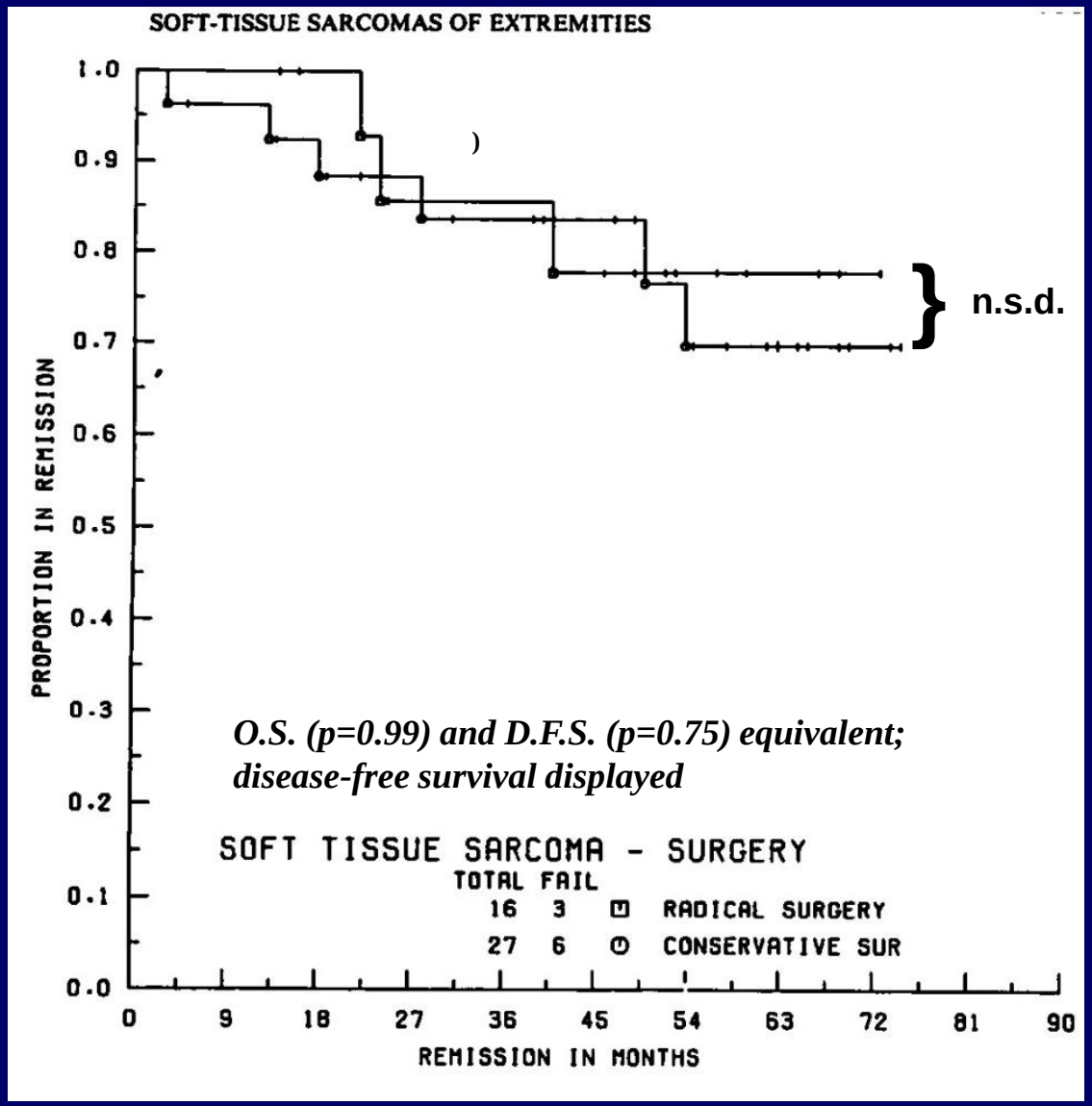
Personalizing local treatment of STS: role of radiotherapy (condensed version)

"Since most soft tissue sarcomas are radio resistant, roentgen therapy as a definitive treatment or in conjunction with surgical treatment is not used."

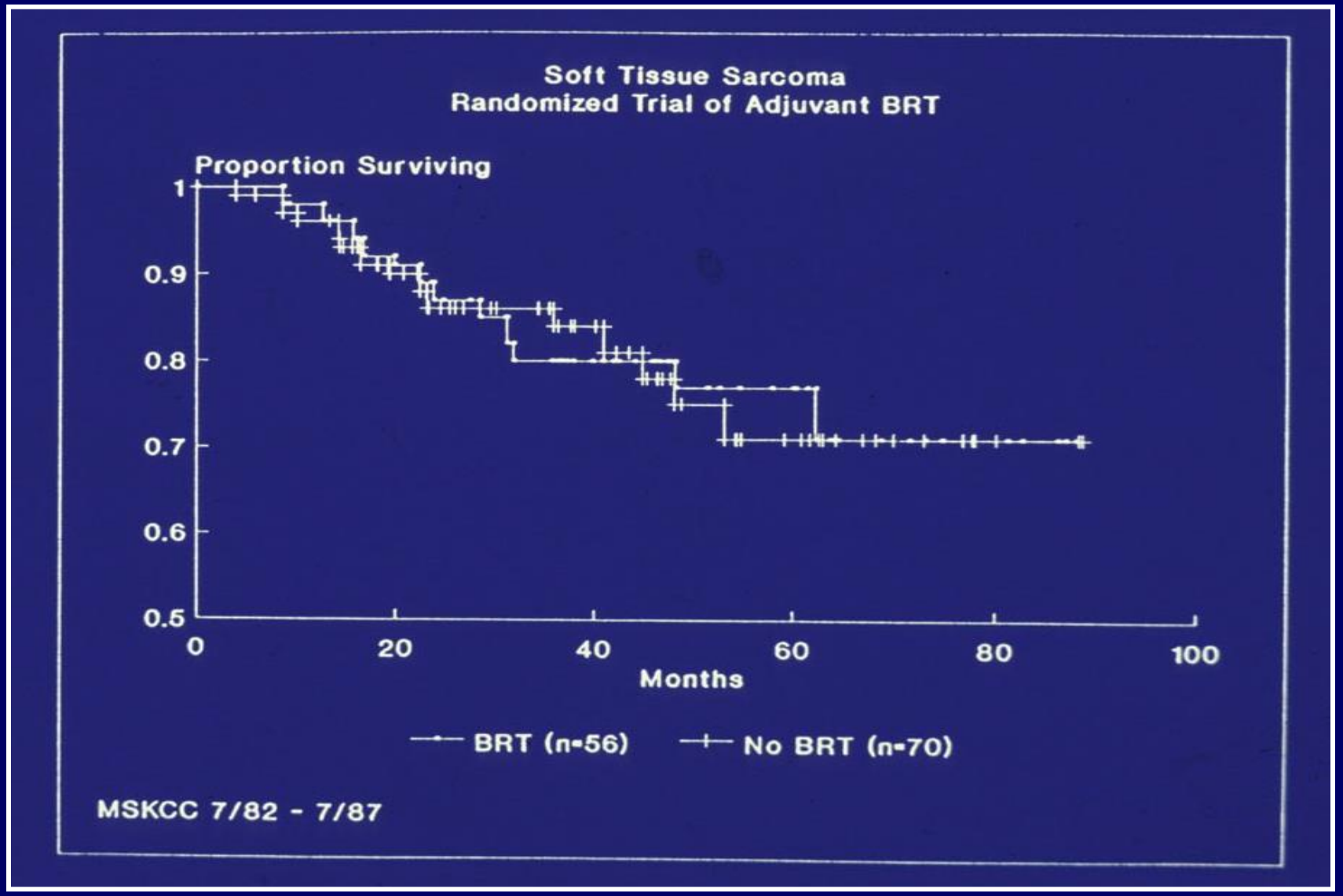
Clark, et. al., 1959

1962: first MD Anderson Cancer Center sarcoma patient treated with external beam radiotherapy

In 1982, Rosenberg report that there was n.s.d. for amputation vs LSS/XRT in extremity STS



We now know that XRT decreases local recurrence



Brennan et al: Ann Surg 1991

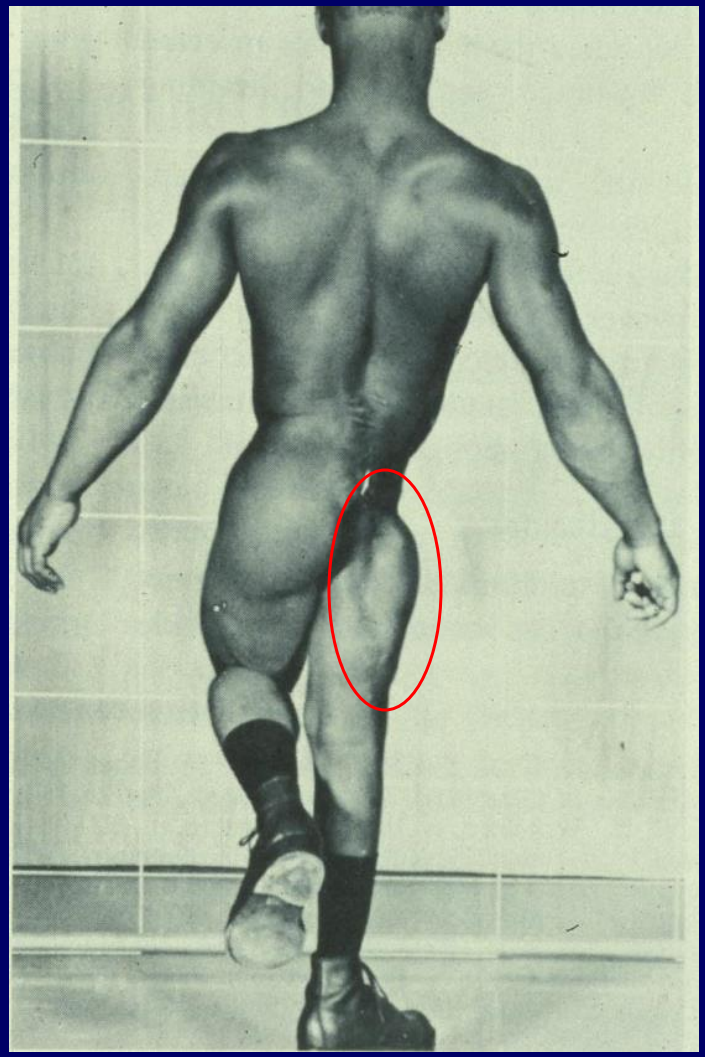
Pre-op vs post-op XRT: the PMH trial

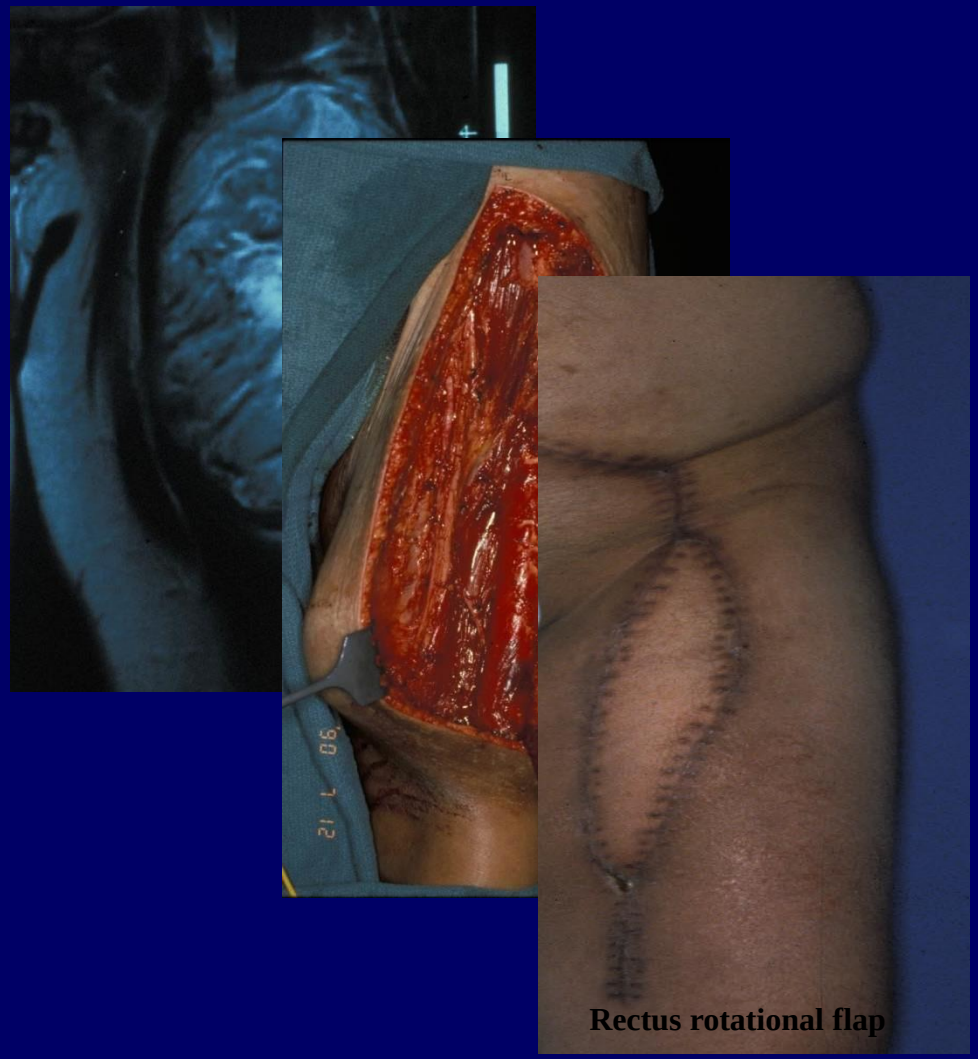
- Randomized pre-op (50 Gy) vs post-op (66Gy); 1995-97
- Early wound complication stop point in pre-op arm
- At five and ten years no difference in d.f.s or o.s.
- Limb function markedly better in pre-op arm (T.E.S.S.)

(O'Sullivan et al; Lancet 2002, 2005)

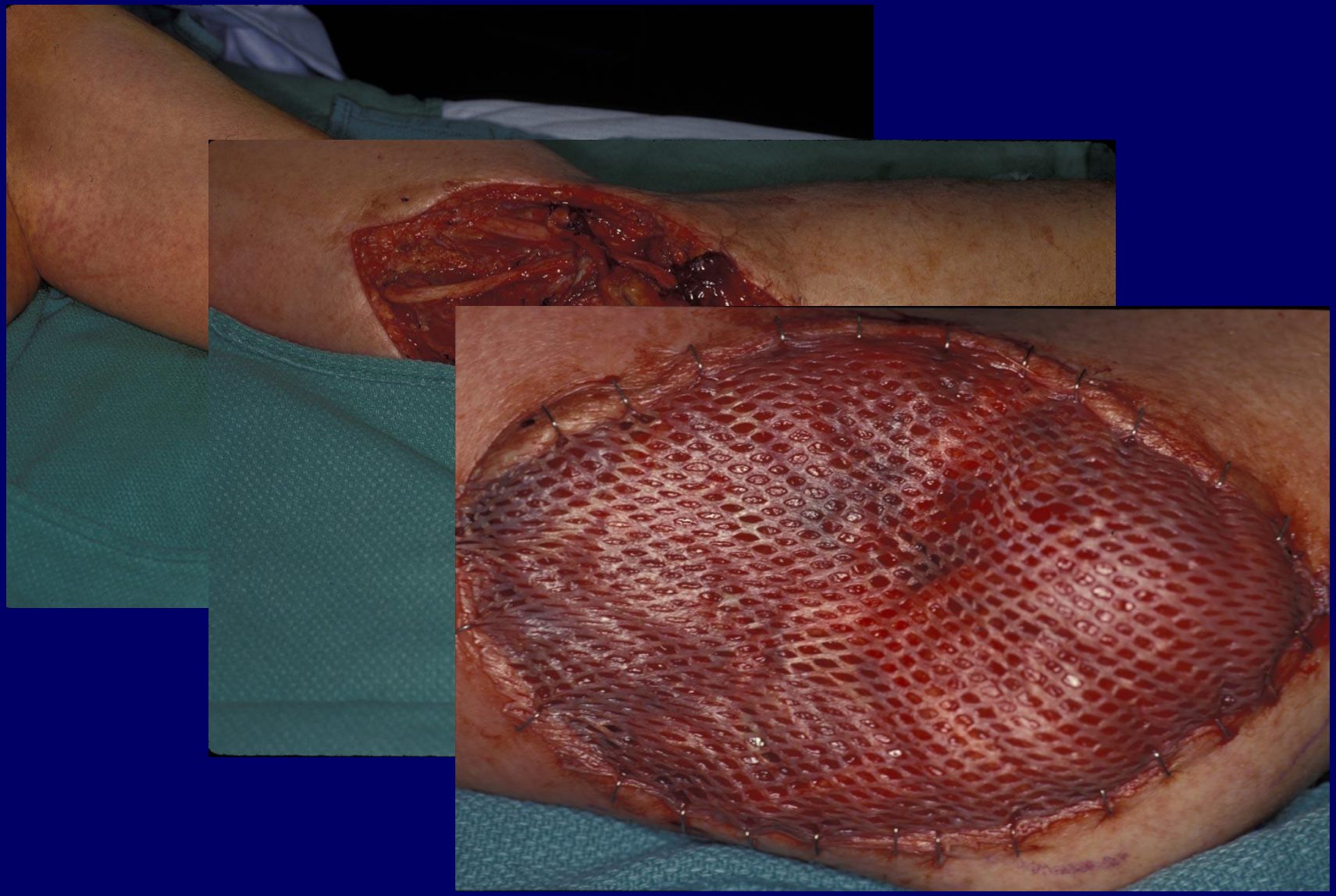
Personalizing local treatment of STS: role of surgery

In the early 1960S radical compartment resection introduced by Enneking; still in use today…

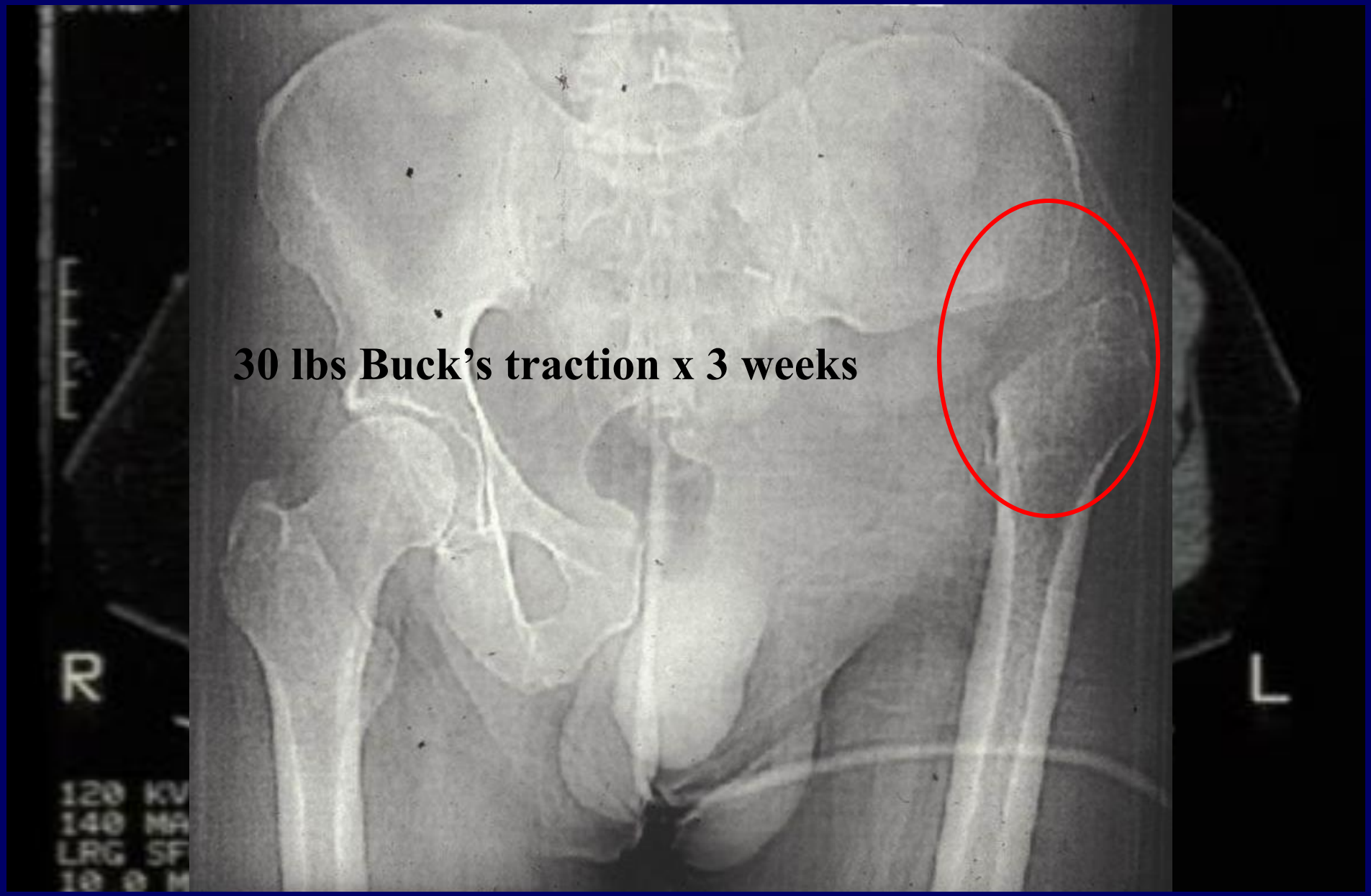




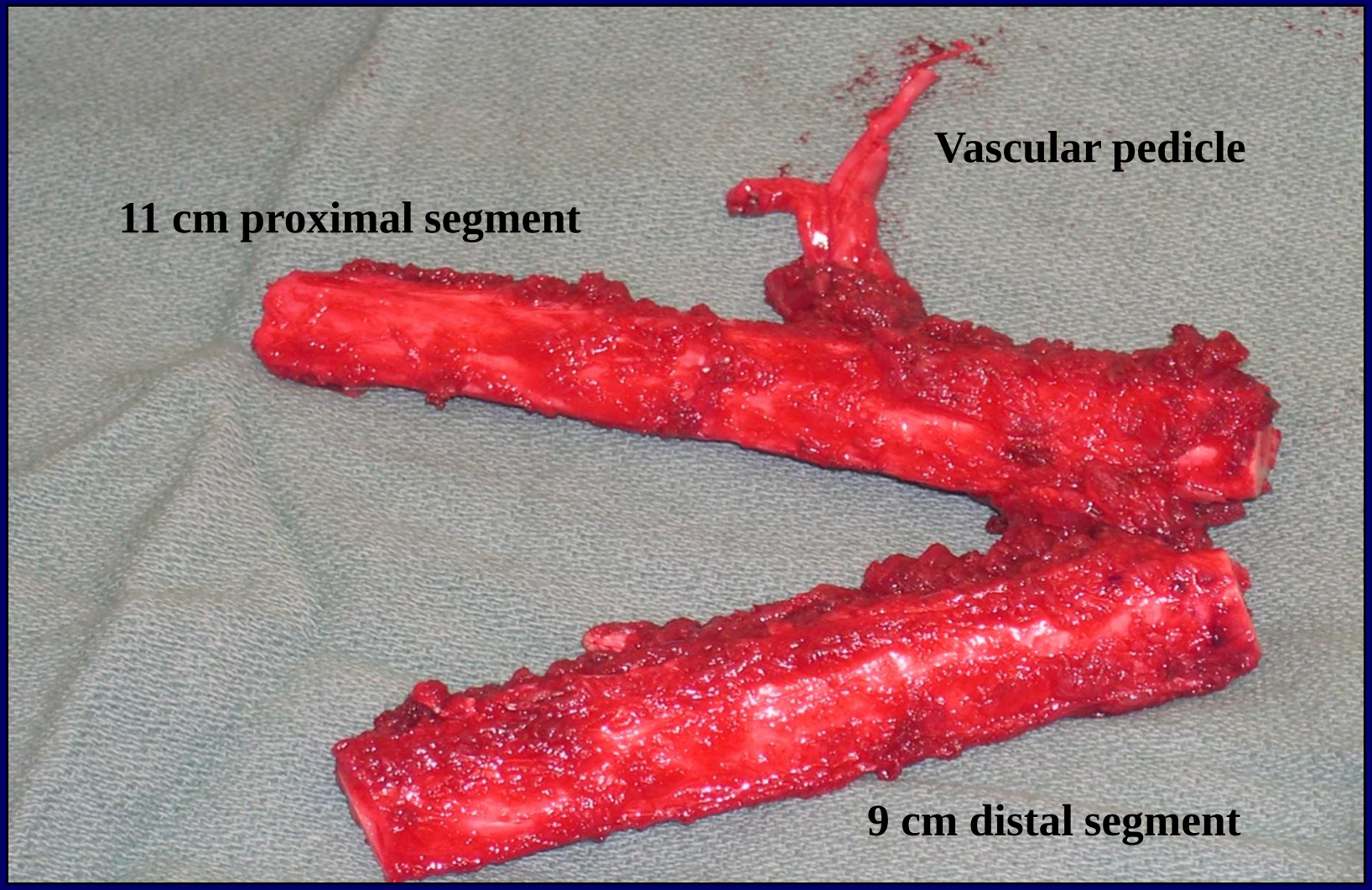
Personalization possibilities enhanced by advent of microvascular reconstruction in the 1990s



Another example: 1980s internal hemipelvectomy



Internal hemipelvectomy, circa 2014: vascularized split fibular graft



Courtesy of Michael Miller, MD and Ehud Mendel, MD OSUCCC

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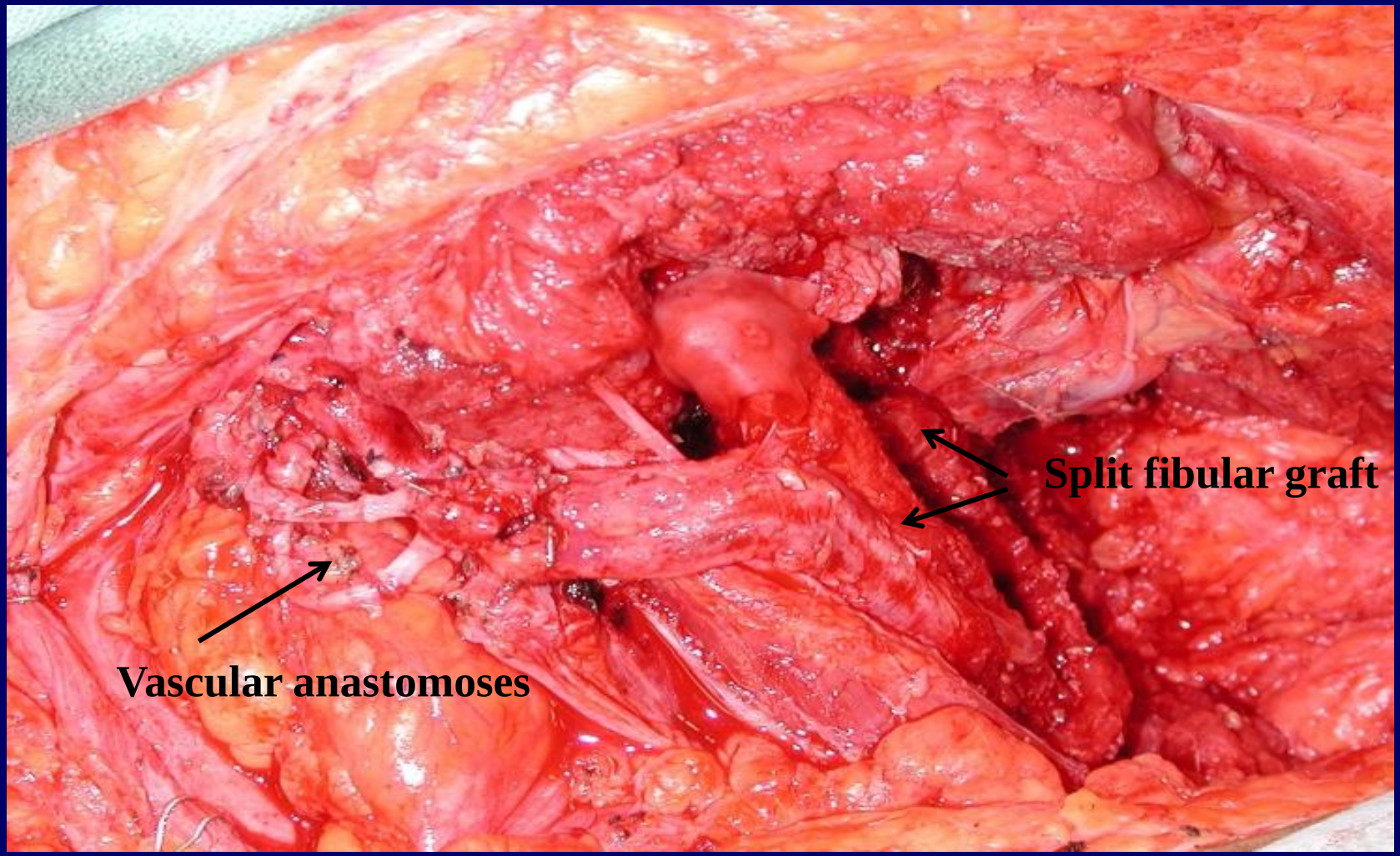

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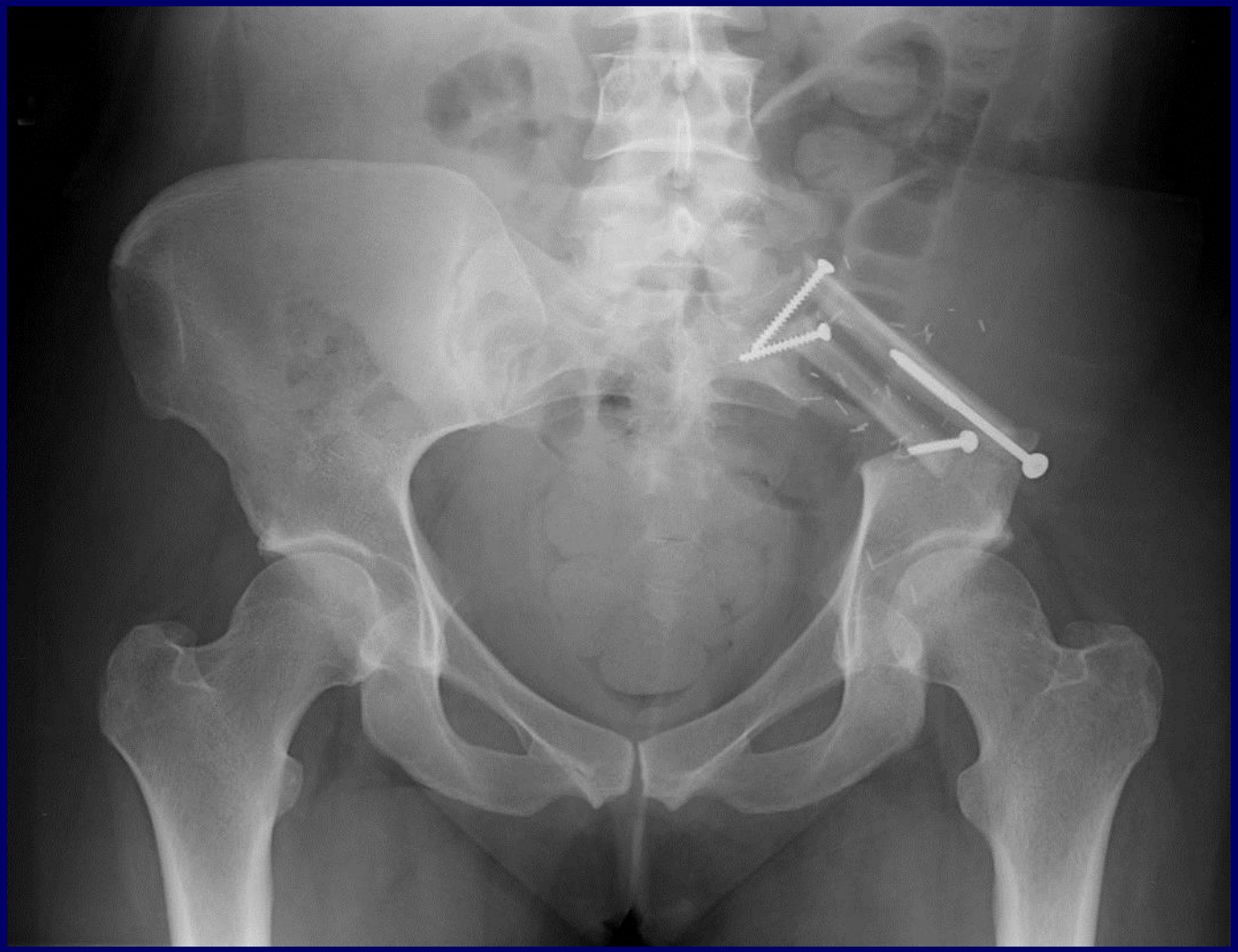

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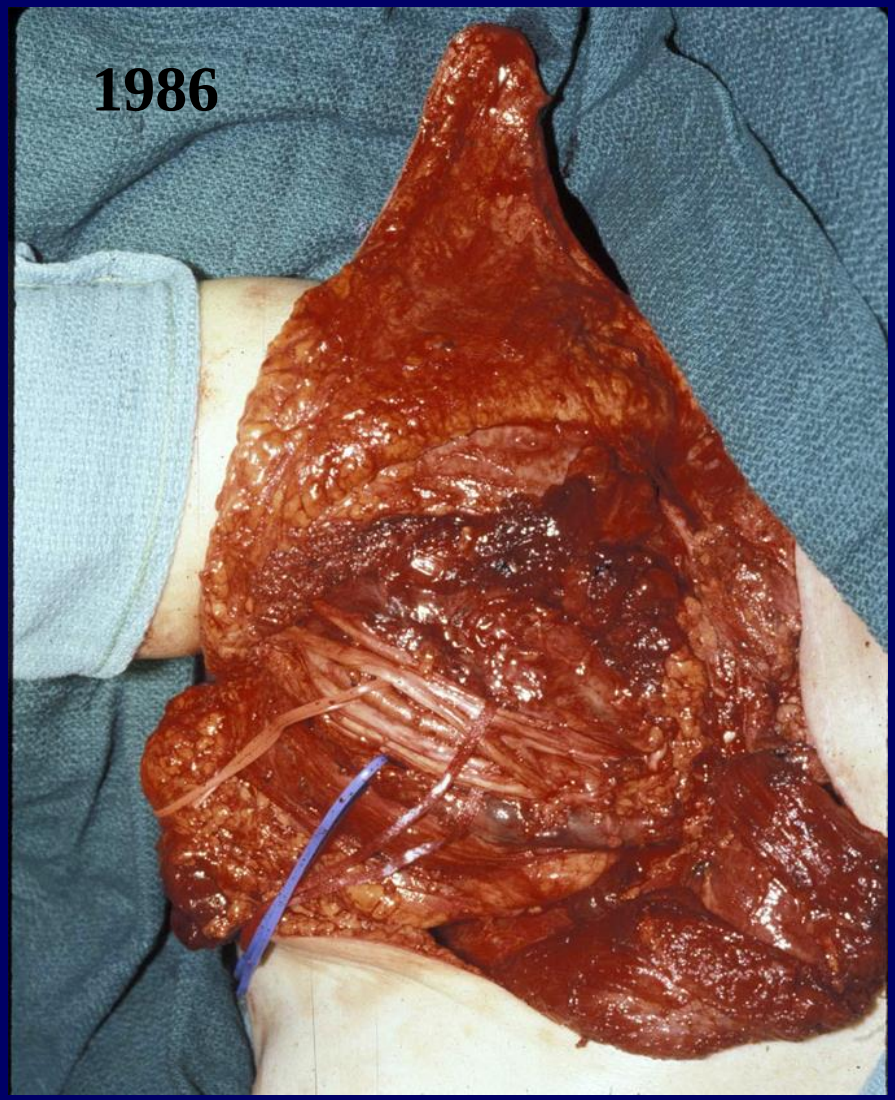
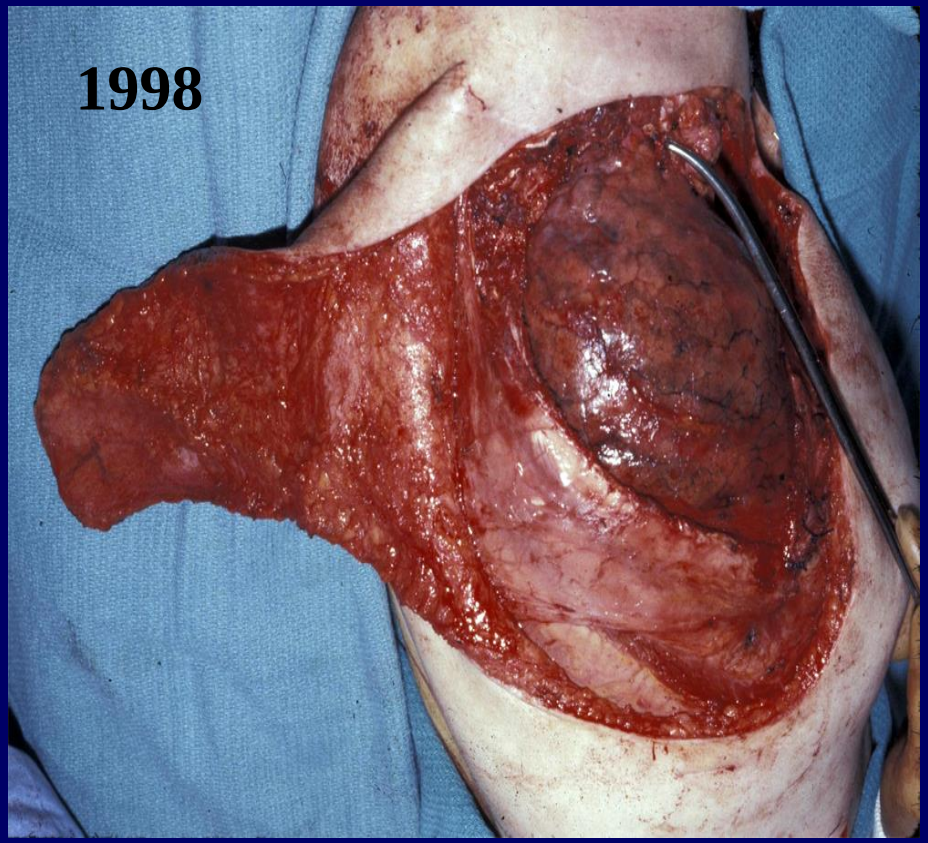
Internal hemipelvectomy, circa 2014

Courtesy of Michael Miller, MD and Ehud Mendel, MD OSUCCC

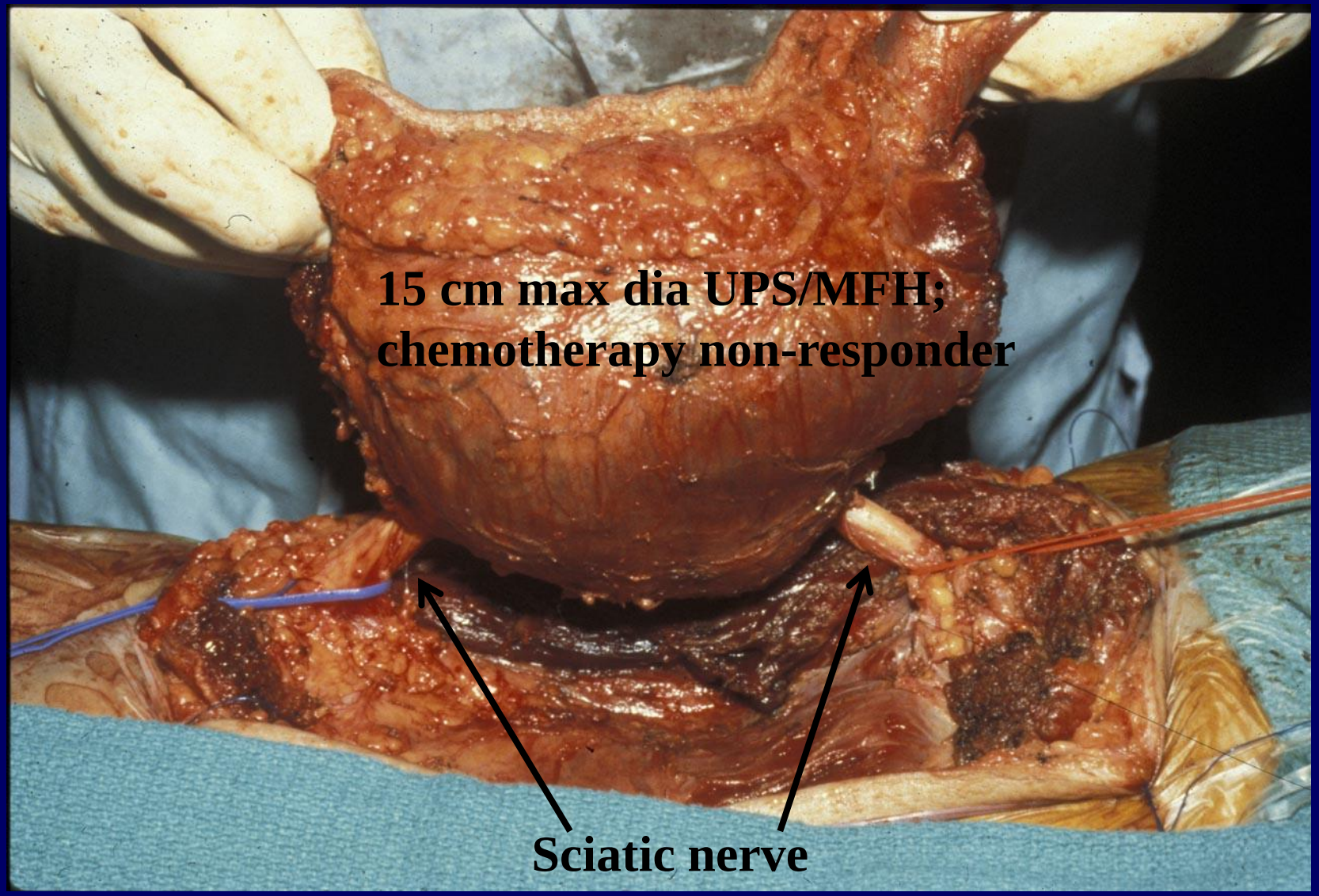
Personalization of local therapies based on (favorable) STS tumor biology



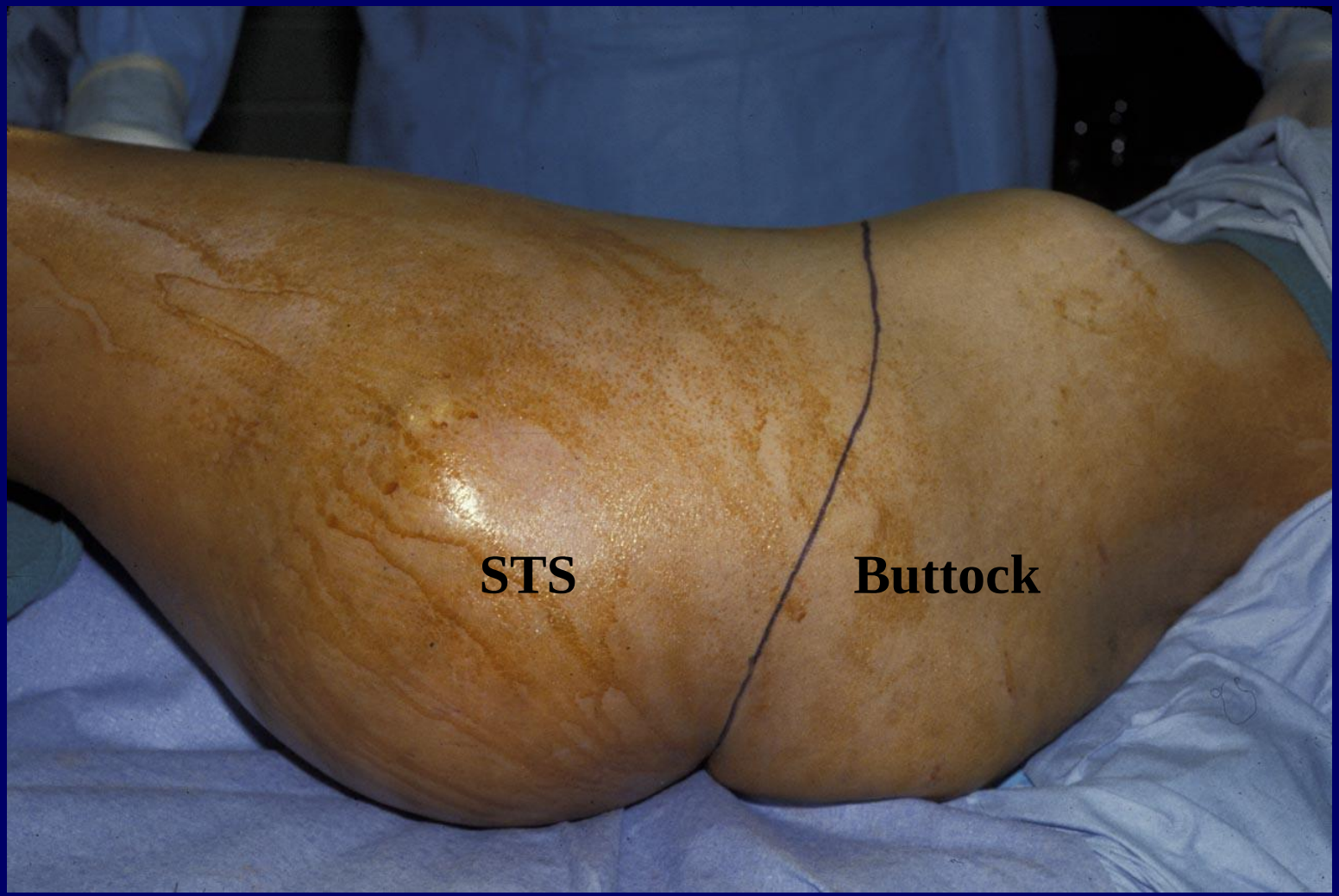
- Favorable histology
- Indolent clinical course



Personalization of local therapies based on (unfavorable) STS tumor biology



The most difficult personalized STS local therapy decisions involve extent of palliative intervention



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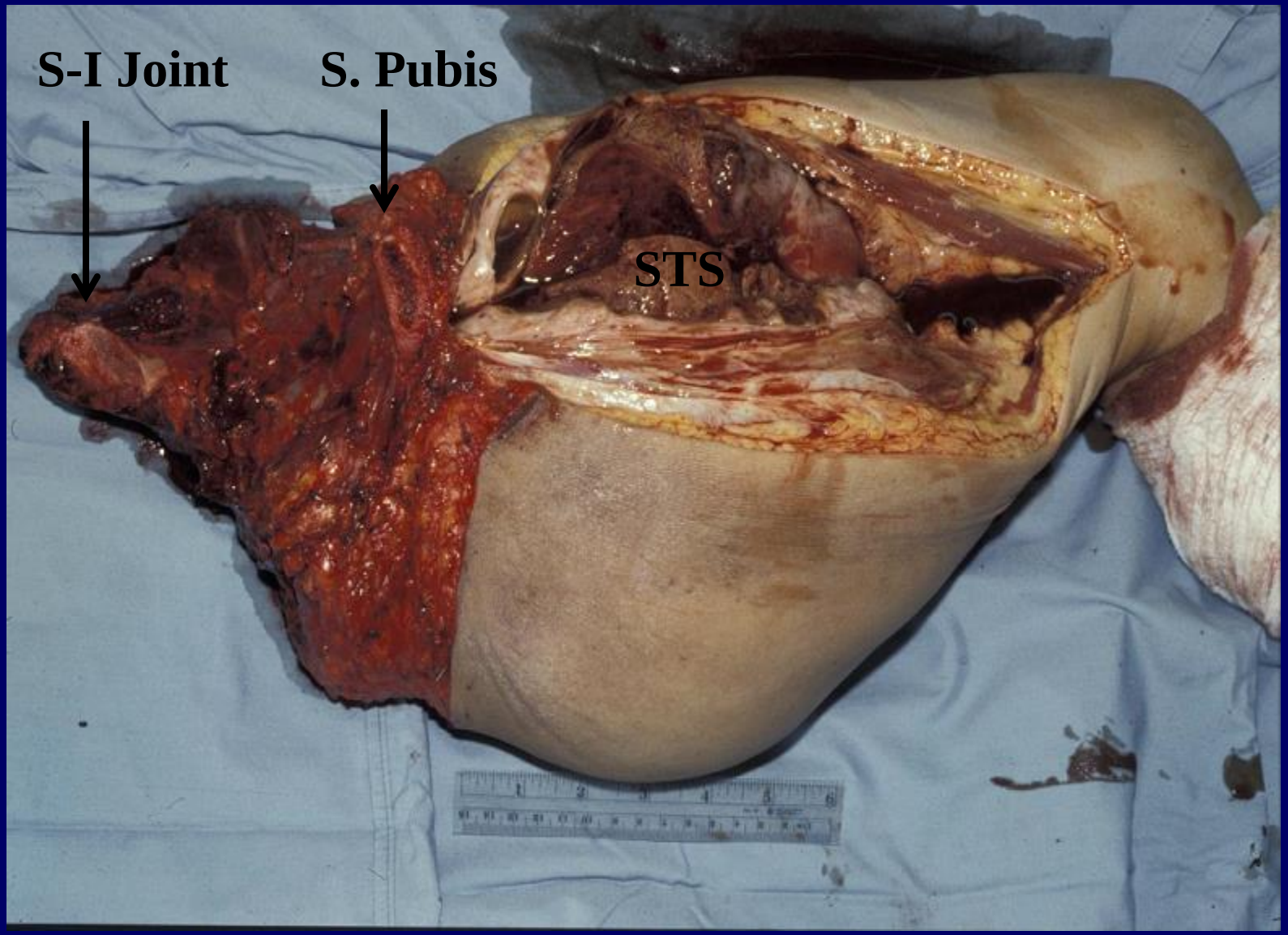
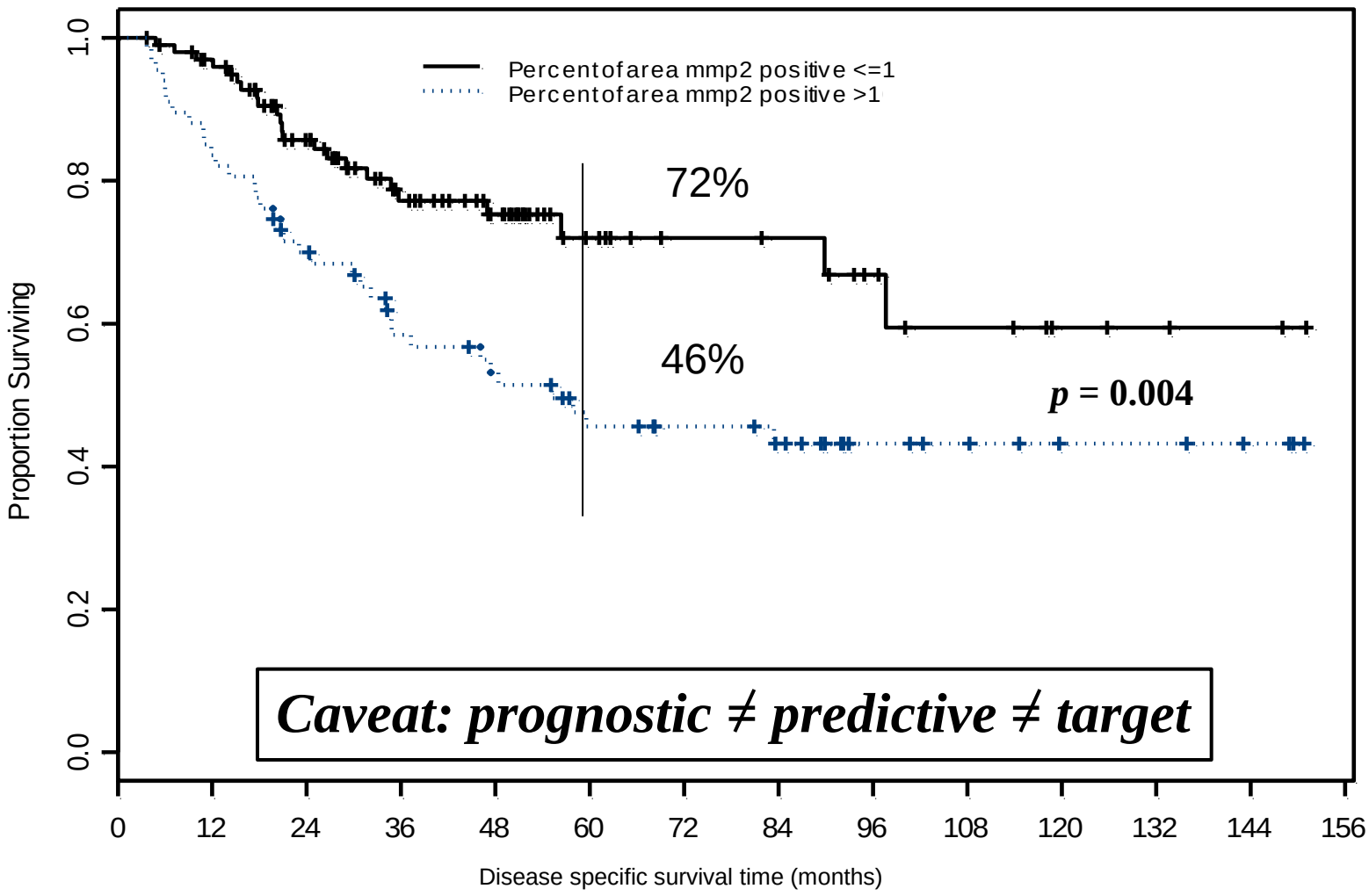


Personalizing local treatment of STS requires prospective multi-disciplinary planning

- Where is the boundary between cure and palliation?
- How should this be decided?
- Who should be involved in this assessment?

Molecular-targeted ext. STS therapy is the future!

TMA-derived data for 257 stage III STS treated at MDACC



Thank you for your attention!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