

SBRT para Sarcomas: Simulação ao tratamento

Elton Leite



XXIV Congresso da
Sociedade Brasileira de
RADIOTERAPIA

17 A 20 DE AGOSTO | 2022 | FLORIANÓPOLIS/SC

VILA NOVA $\int$ TAR
REDE D'OR



INSTITUTO DO
CÂNCER
DO ESTADO DE
SÃO PAULO
OCTAVIO FRIAS DE OLIVEIRA

SBRT para Sarcomas: ~~Simulação~~ ao tratamento Indicação Elton Leite



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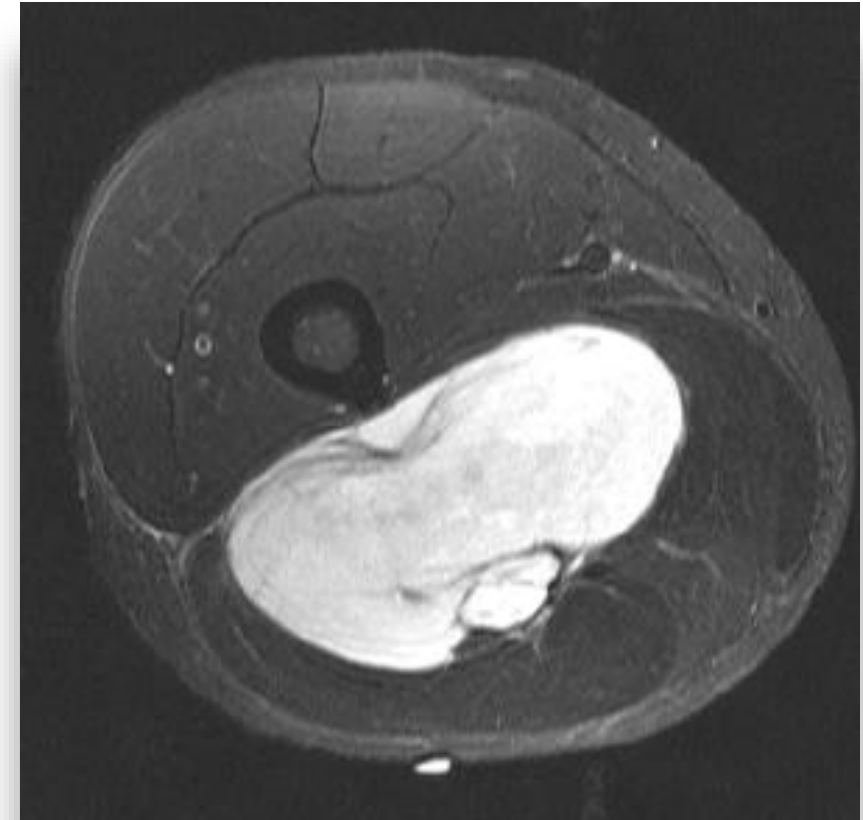
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Sarcomas de partes moles

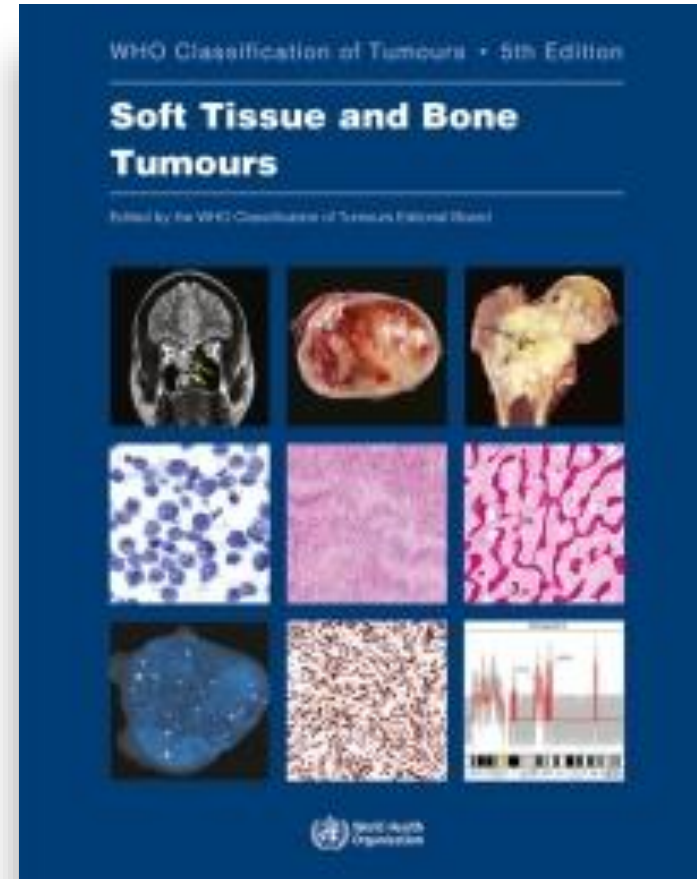
- Estimativa 2022: 13.190 casos nos EUA
- 0.7% de todos os tipos de câncer
- 5130 mortes estimadas
- 0.8% de todas as mortes por câncer
- Cirurgia – tratamento principal



Sarcomas de partes moles

Apresentação histológica

- Leiomiossarcoma 23,9%
- Sarcoma indiferenciado 17,1%
- Lipossarcoma 11,5%,
- Dermatofibrosssarcoma 10,5%,
- Rabdomiossarcomas 4,6%
- Angiossarcoma 4%

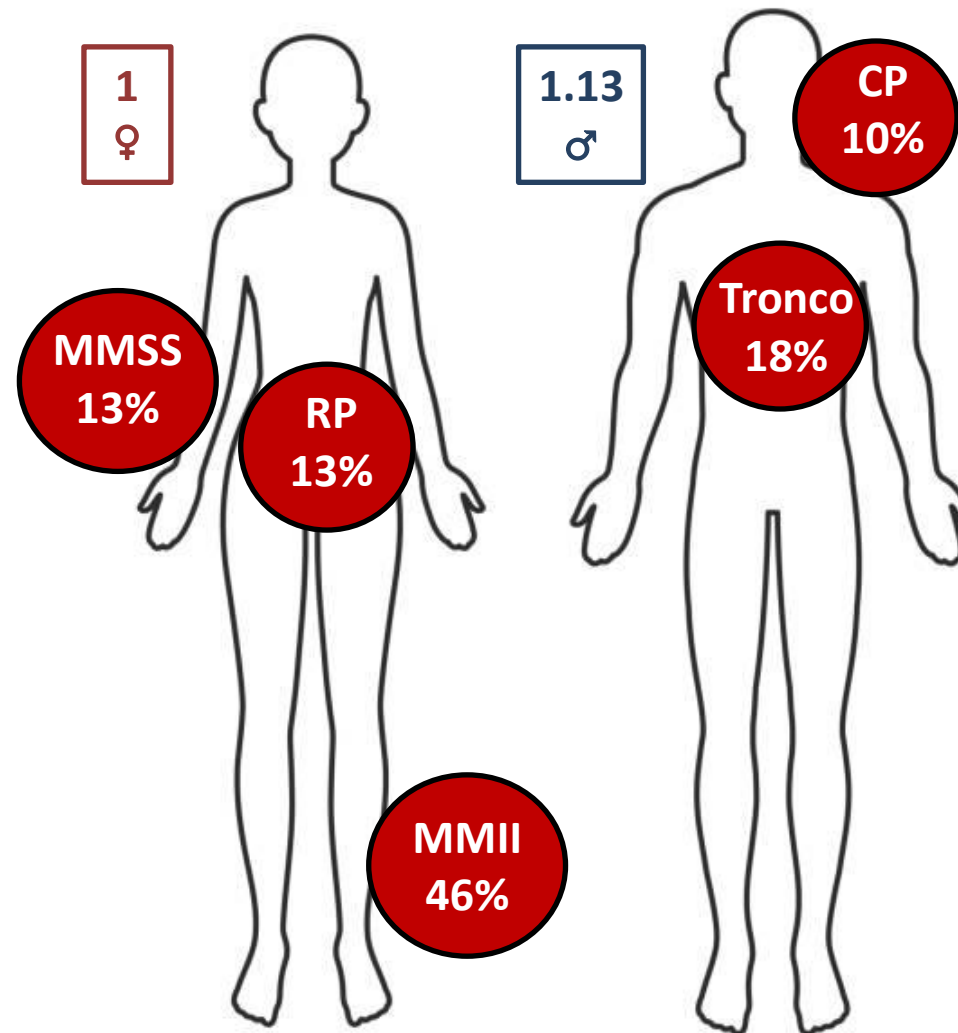


Sarcomas de partes moles

- Doença heterogênea
- 10% metástases ao diagnóstico
- Sítio mais comum de metástase: pulmão
- Progressão à distância: 25% (50% - alto grau)

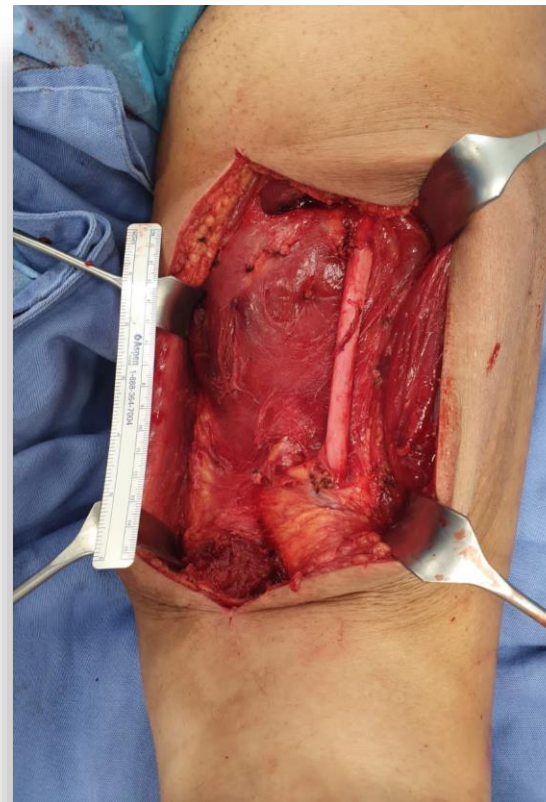


Sarcomas de partes moles

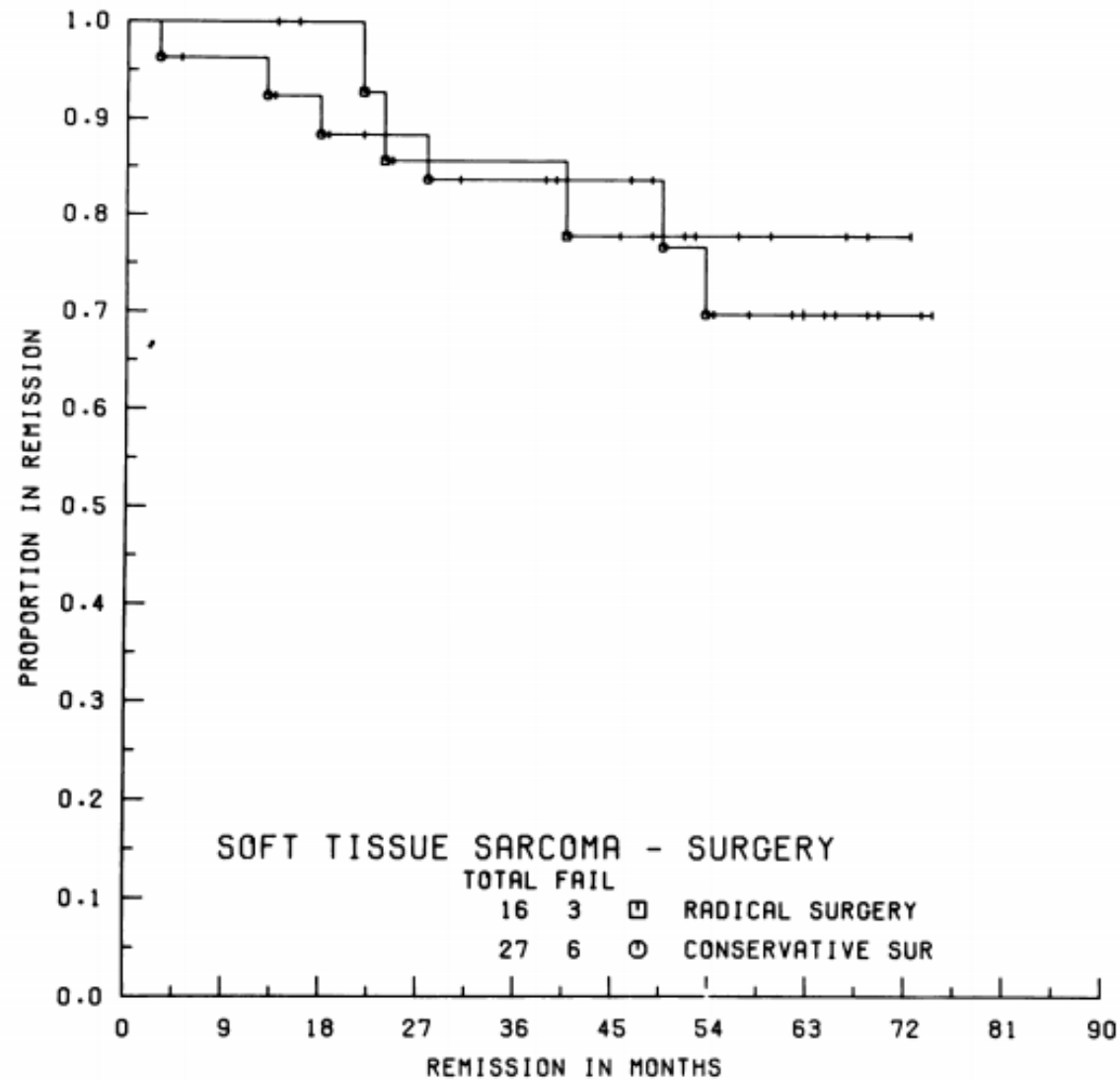


Cirurgia

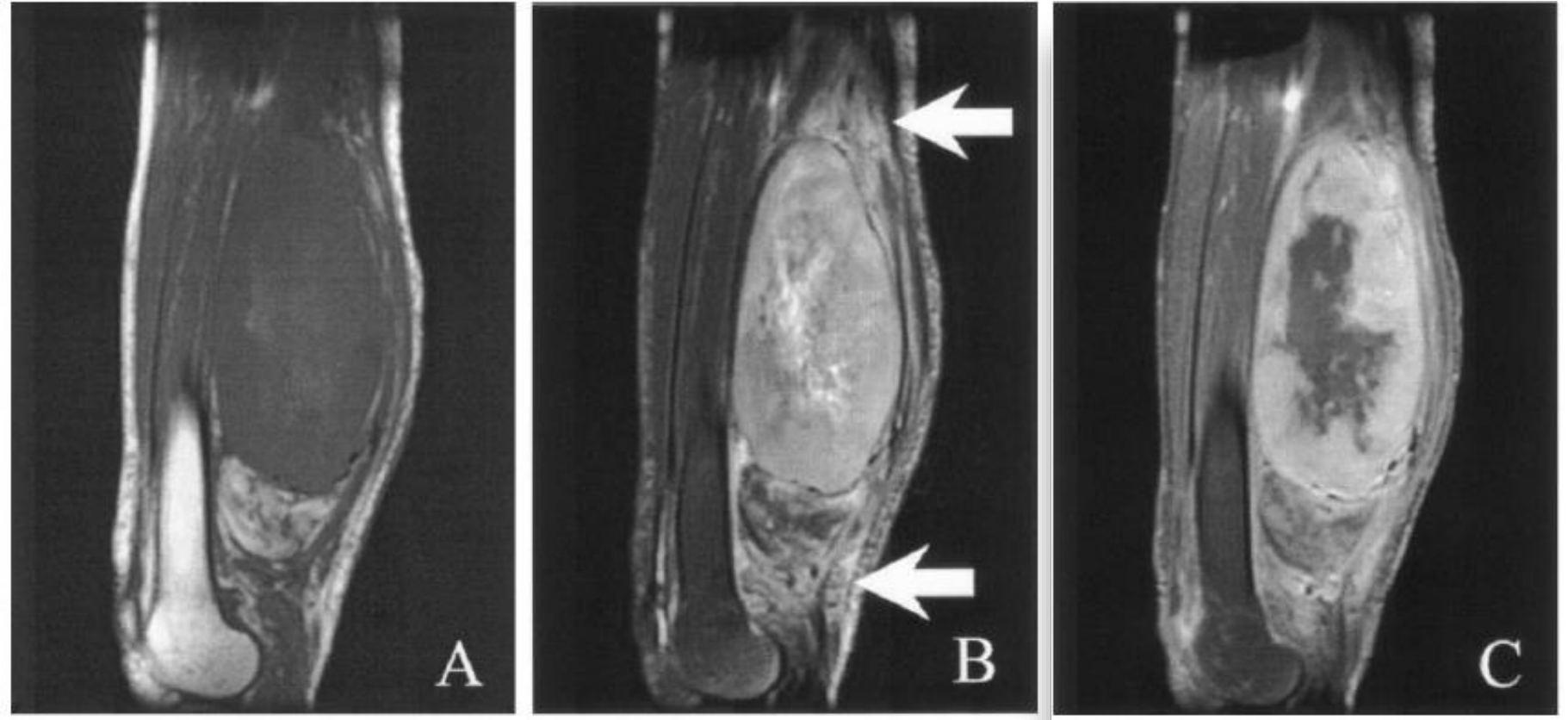
- **Principal** modalidade de tratamento
- Padrão atual: cirurgia **conservadora** do membro
- Ressecção em bloco com margens programadas de **1-2cm** ao redor da pseudocápsula
- Margens livres: principal fator **prognóstico**



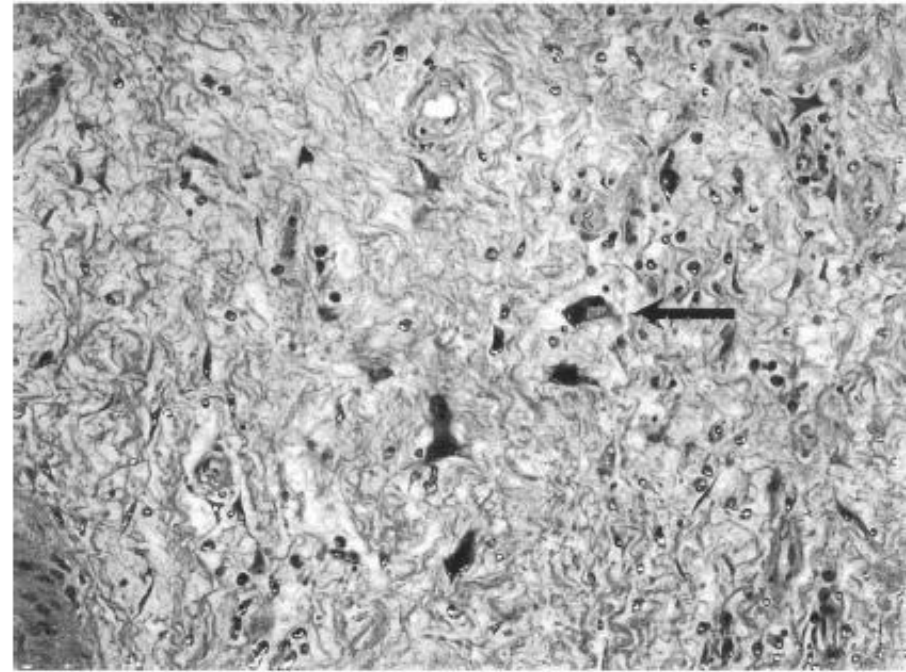
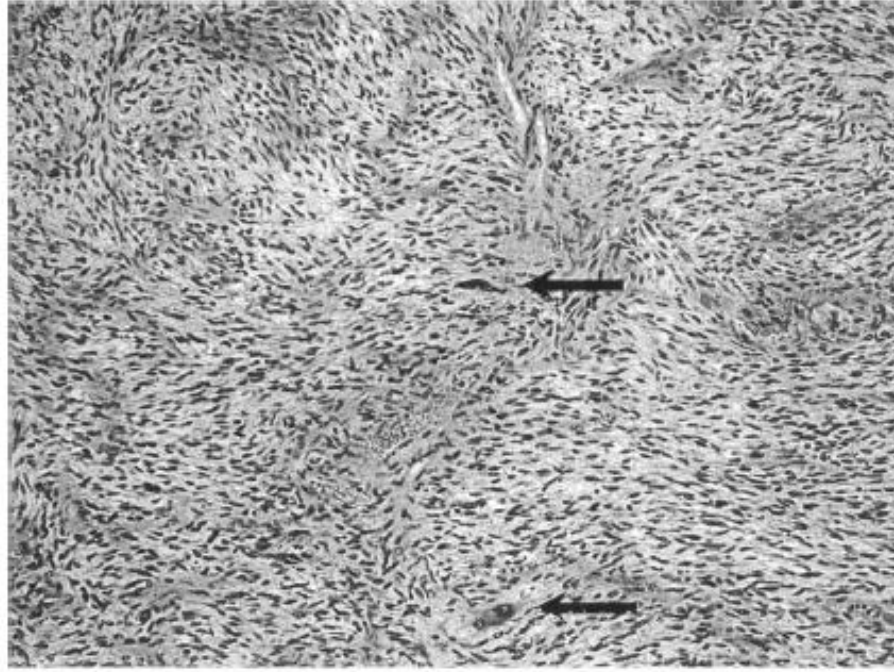
Amputação vs Tratamento conservador



Margens



Margens



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CIRURGIA

PISTERS et al.

OBSERVAÇÃO

BRAQUITERAPIA

CIRURGIA

YANG et al.

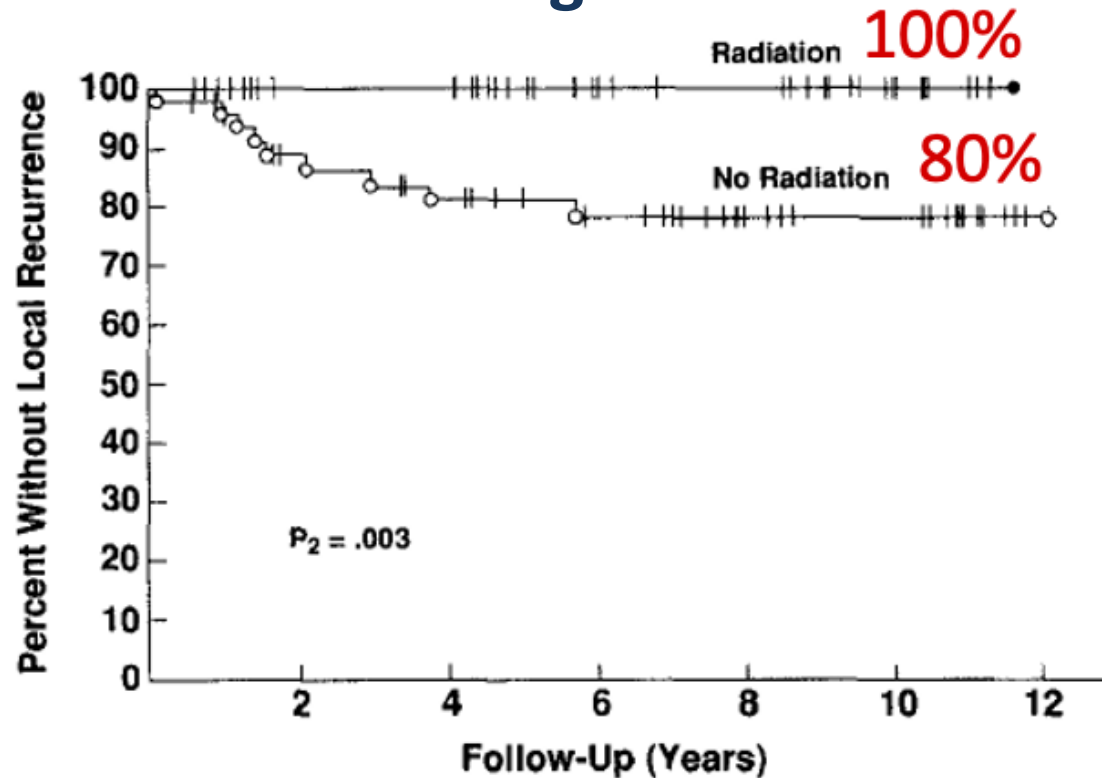
OBSERVAÇÃO

RADIOTERAPIA EXTERNA

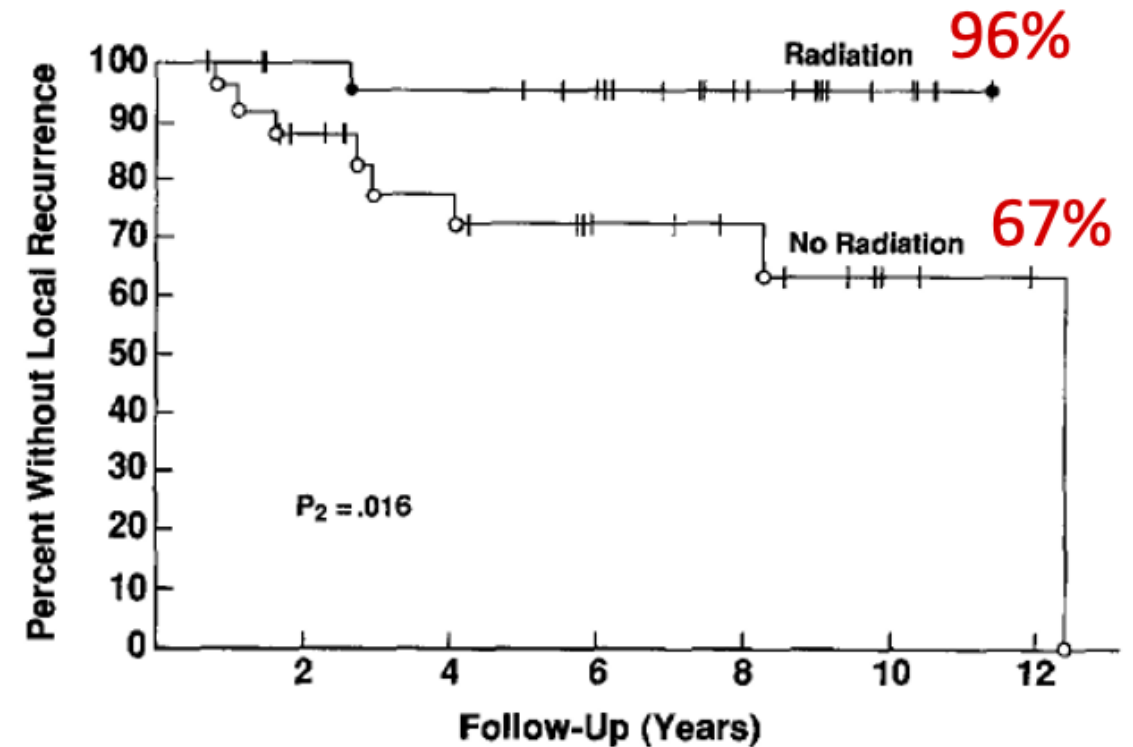


Radioterapia externa

Alto grau

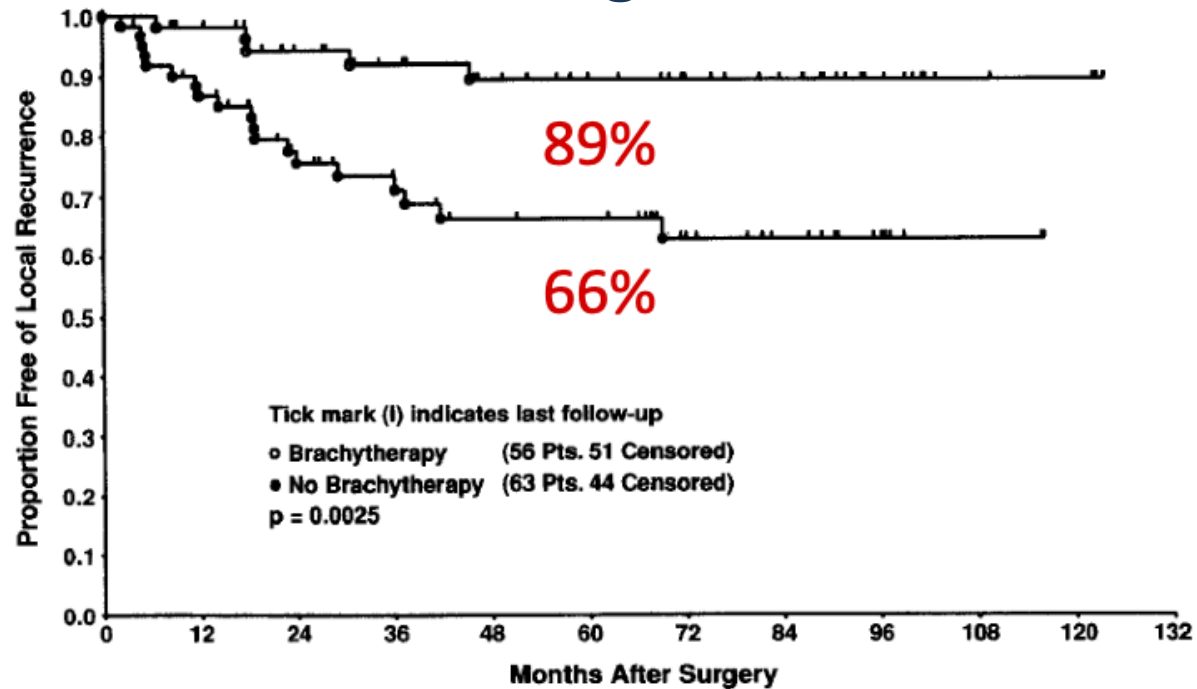


Baixo grau

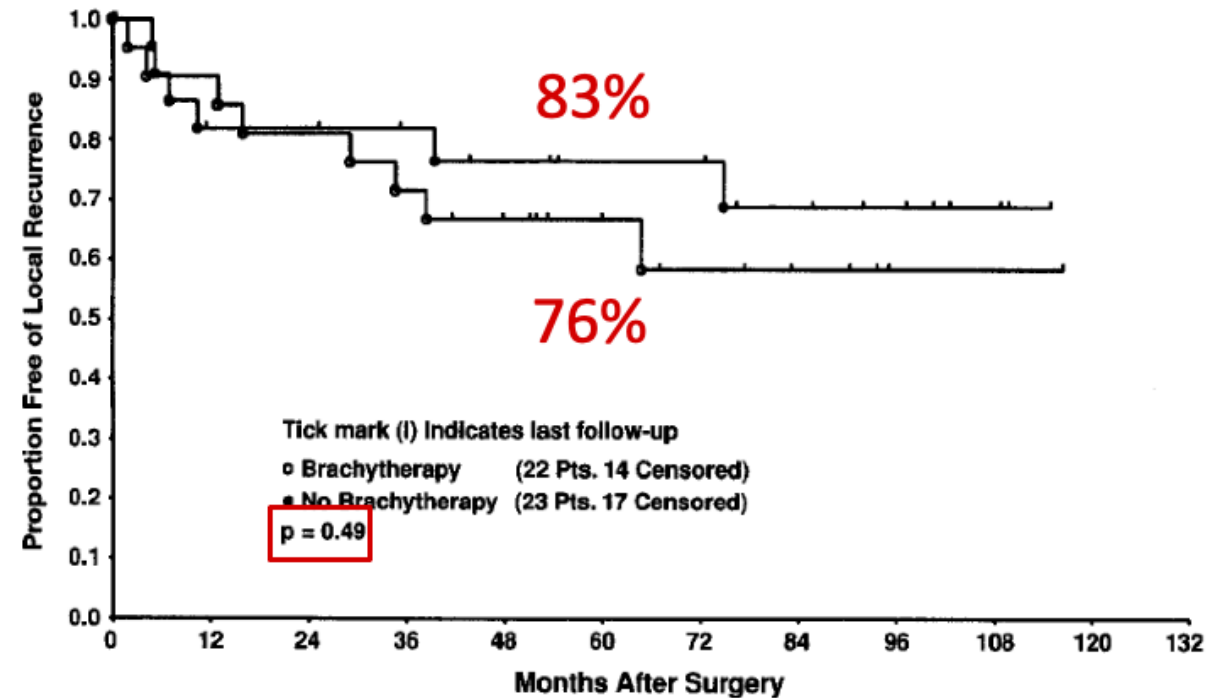


Braquiterapia

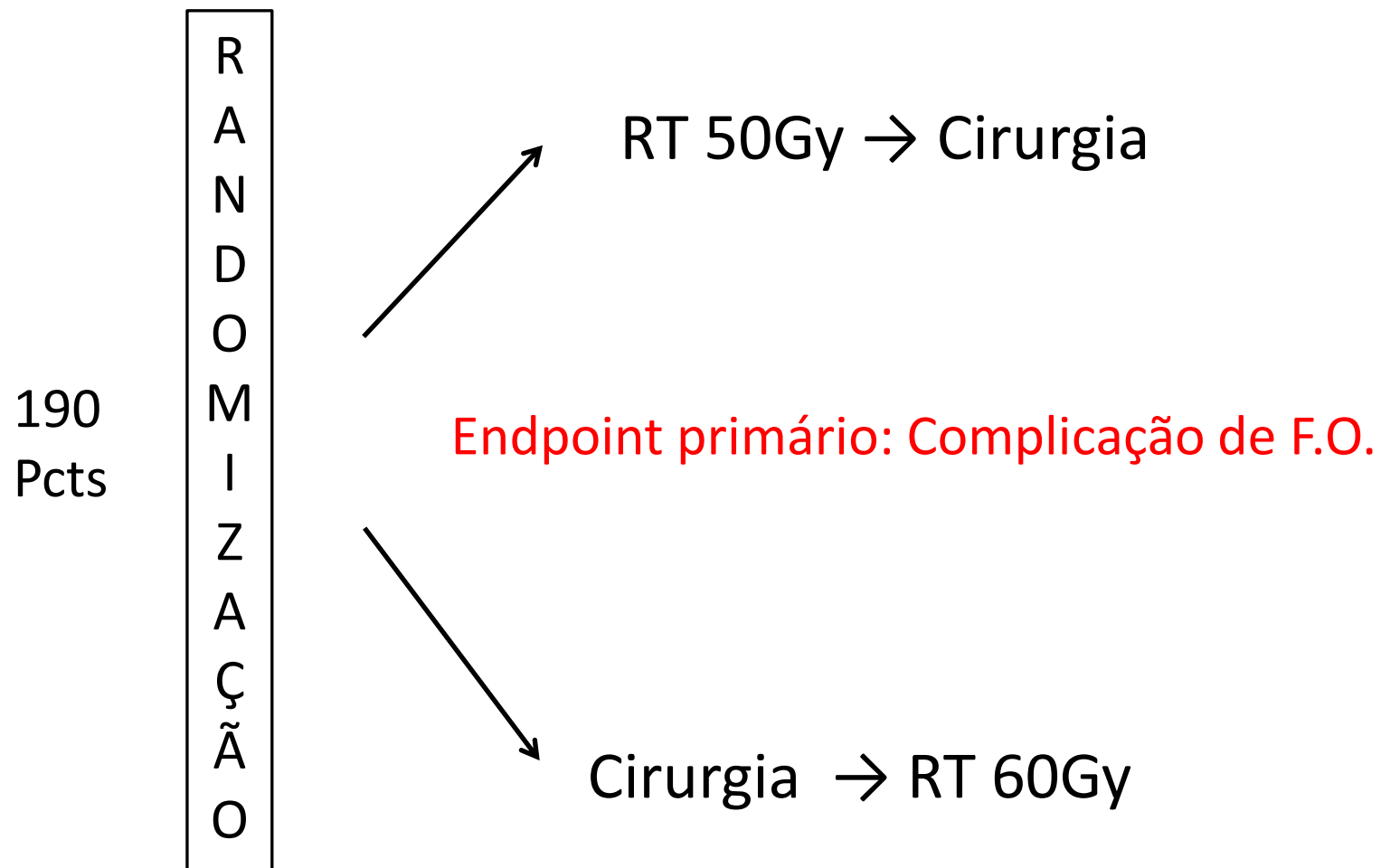
Alto grau



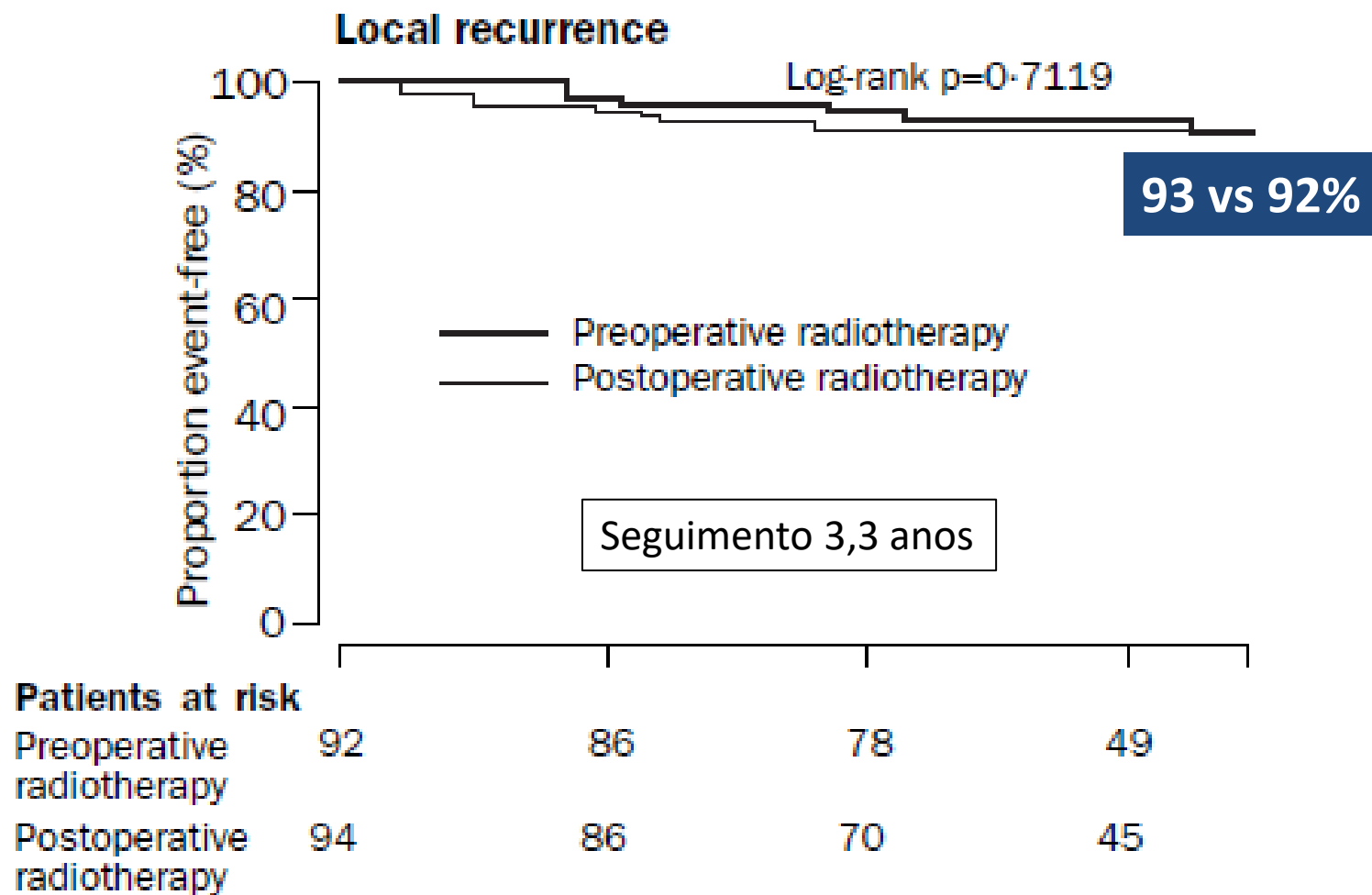
Baixo grau



RT PRÉ vs PÓS op



RT PRÉ vs PÓS op



RT PRÉ vs PÓS op

	Preoperative (n=88)	Postoperative (n=94)
Wound complications*	35%	17%
Yes		
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	11 (35%)	7 (44%)
>6 weeks from wound breakdown‡		
Readmission for wound care§	1 (3%)	0
No complications	57 (65%)	78 (83%)

	Preoperative (n=88)	Postoperative (n=94)
Type of wound closure		
Primary	58 (66%)	72 (77%)
Vascularised tissue	25 (28%)	19 (20%)
Split skin graft	5 (6%)	3 (3%)
Wound complication by anatomical site		
Upper arm		
No	9 (90%)	11 (100%)
Yes	1 (10%)	0
Lower arm		
No	8 (100%)	8 (100%)
Yes	0	0
Upper leg		
No	24 (55%)	39 (72%)
Yes	20 (45%)	15 (28%)
Lower leg		
No	16 (62%)	20 (95%)
Yes	10 (38%)	1 (5%)
Wound complication by type of wound reconstruction		
Primary closure		
No	38 (66%)	58 (81%)
Yes	20 (34%)	14 (19%)
Non-primary closure		
No	19 (63%)	20 (91%)
Yes	11 (37%)	2 (9%)

MMII

43%

21%



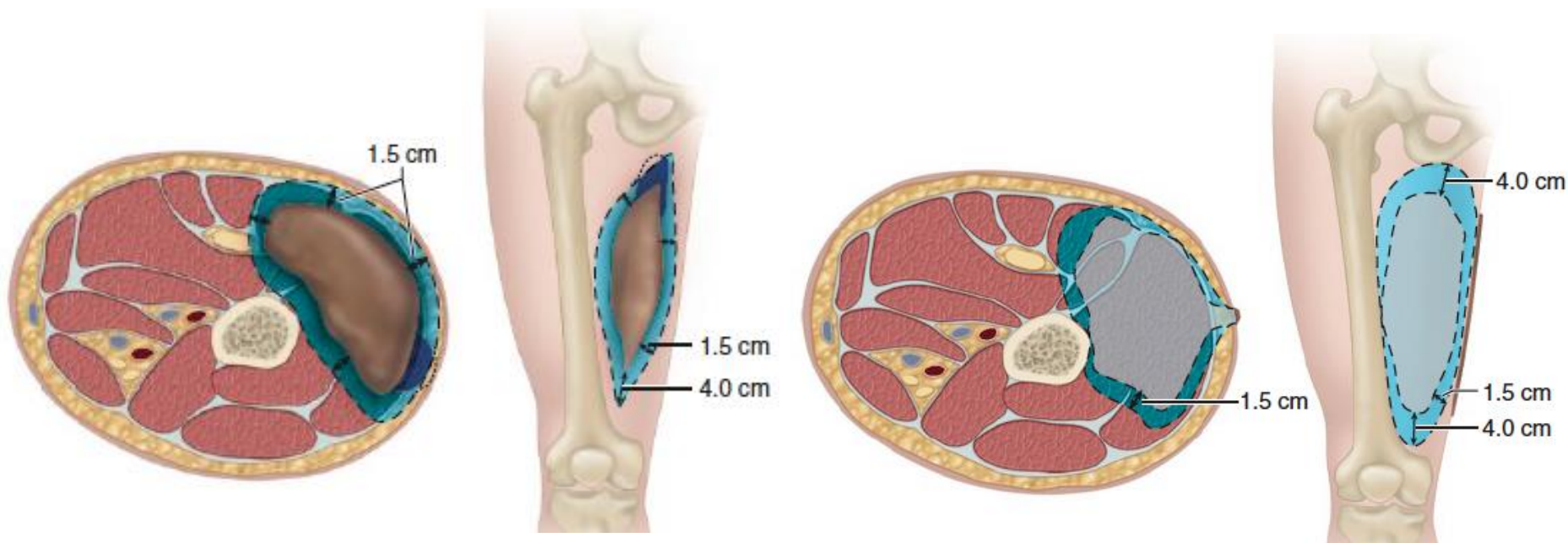
RT PRÉ vs PÓS op

Análise subsequente: FUNÇÃO

Grade ≥ 2	<u>Pre-Op</u>	<u>Post-Op</u>	
Fibrosis	31.5%	48.2%	p=0.07
Edema	15.1%	23.2%	p=ns
Joint stiffness	17.8%	23.2%	

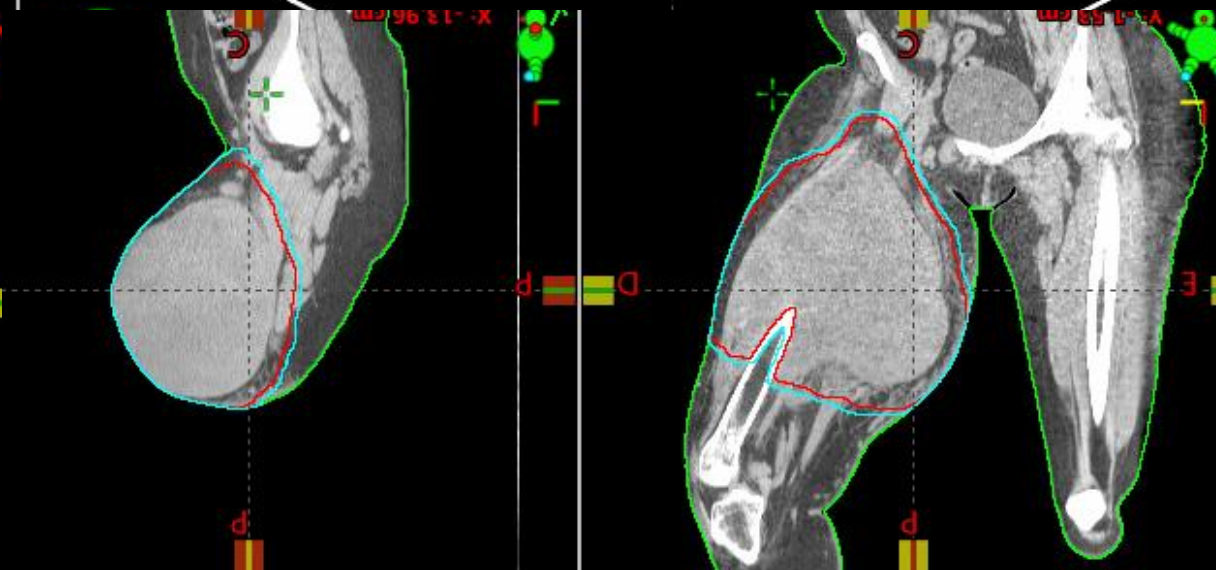
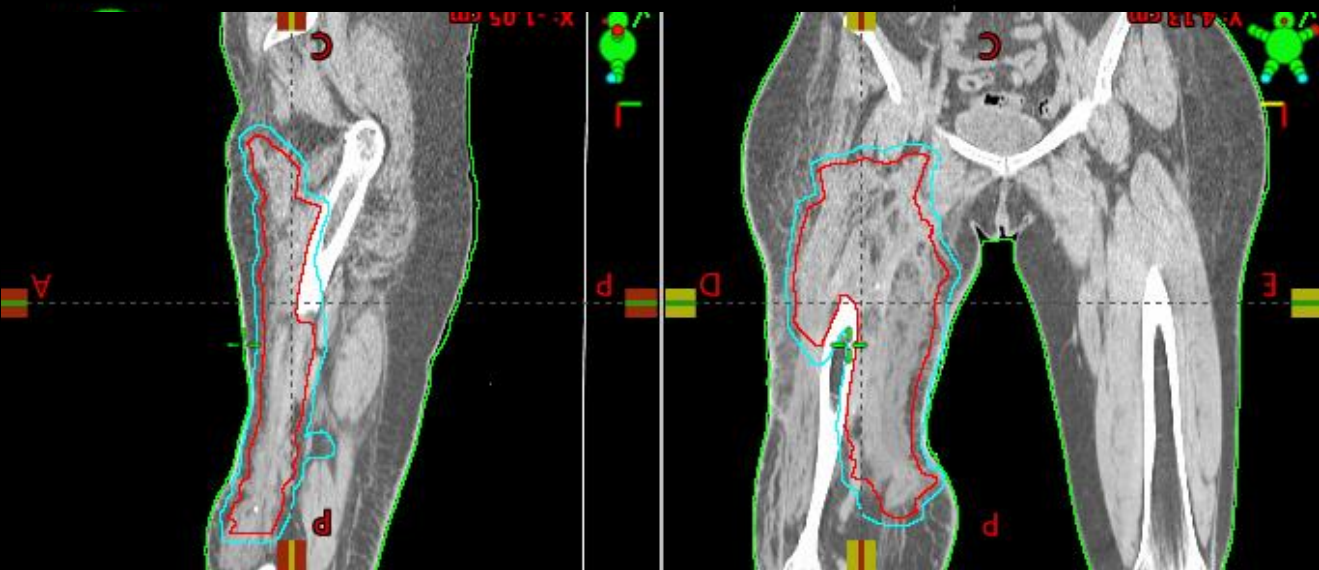
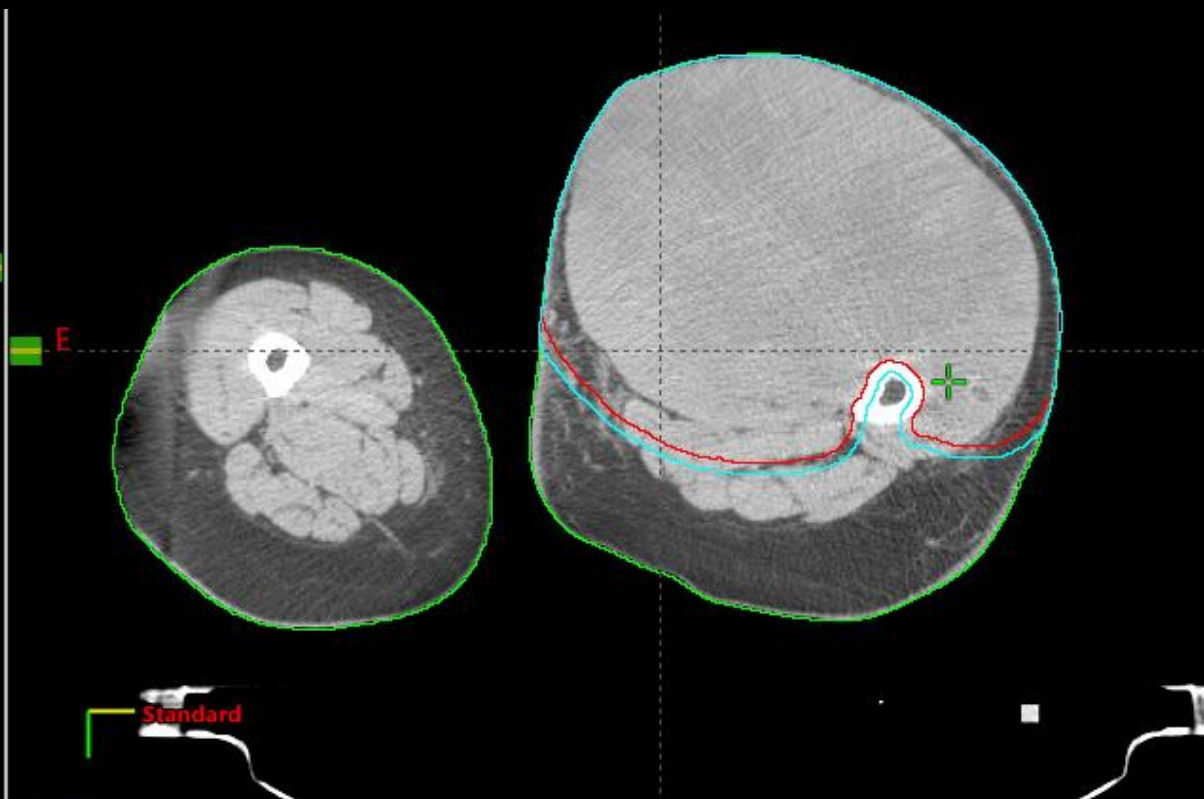
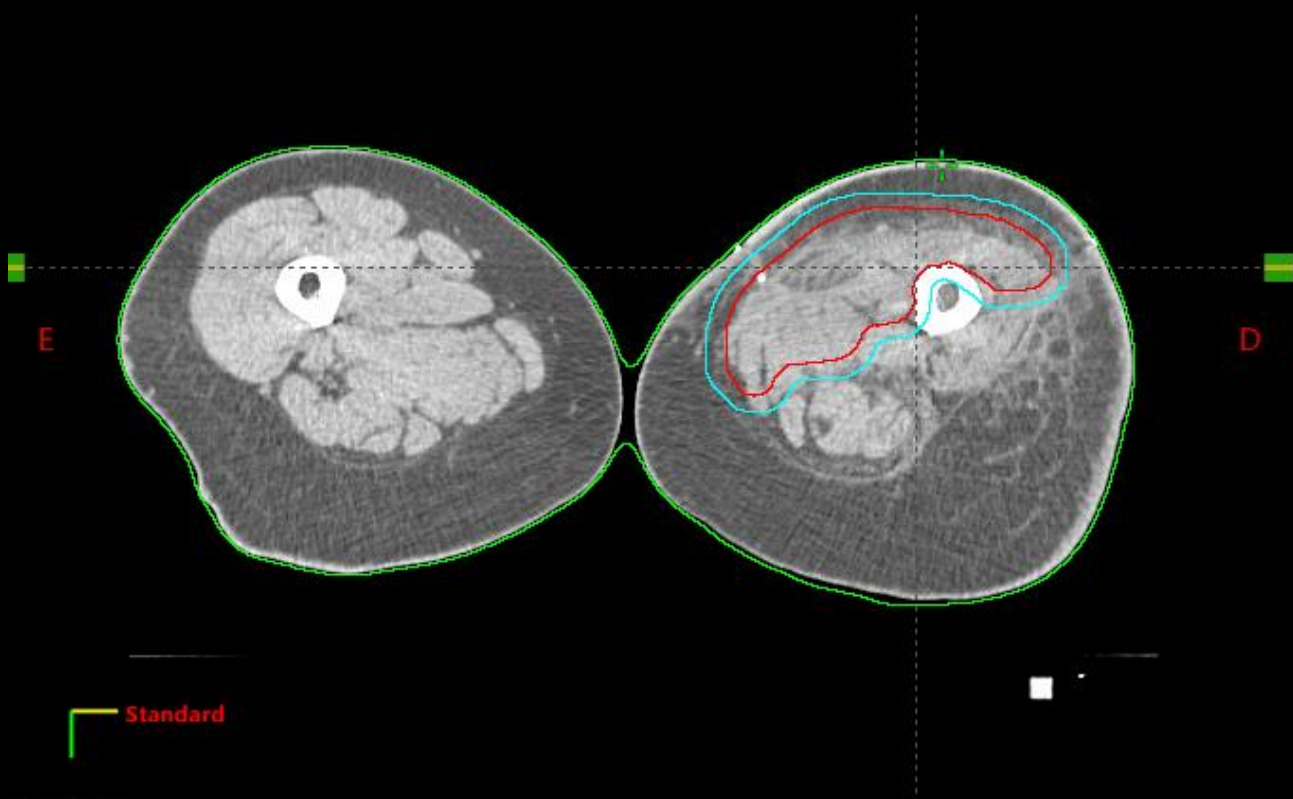
RT PRÉ vs PÓS op

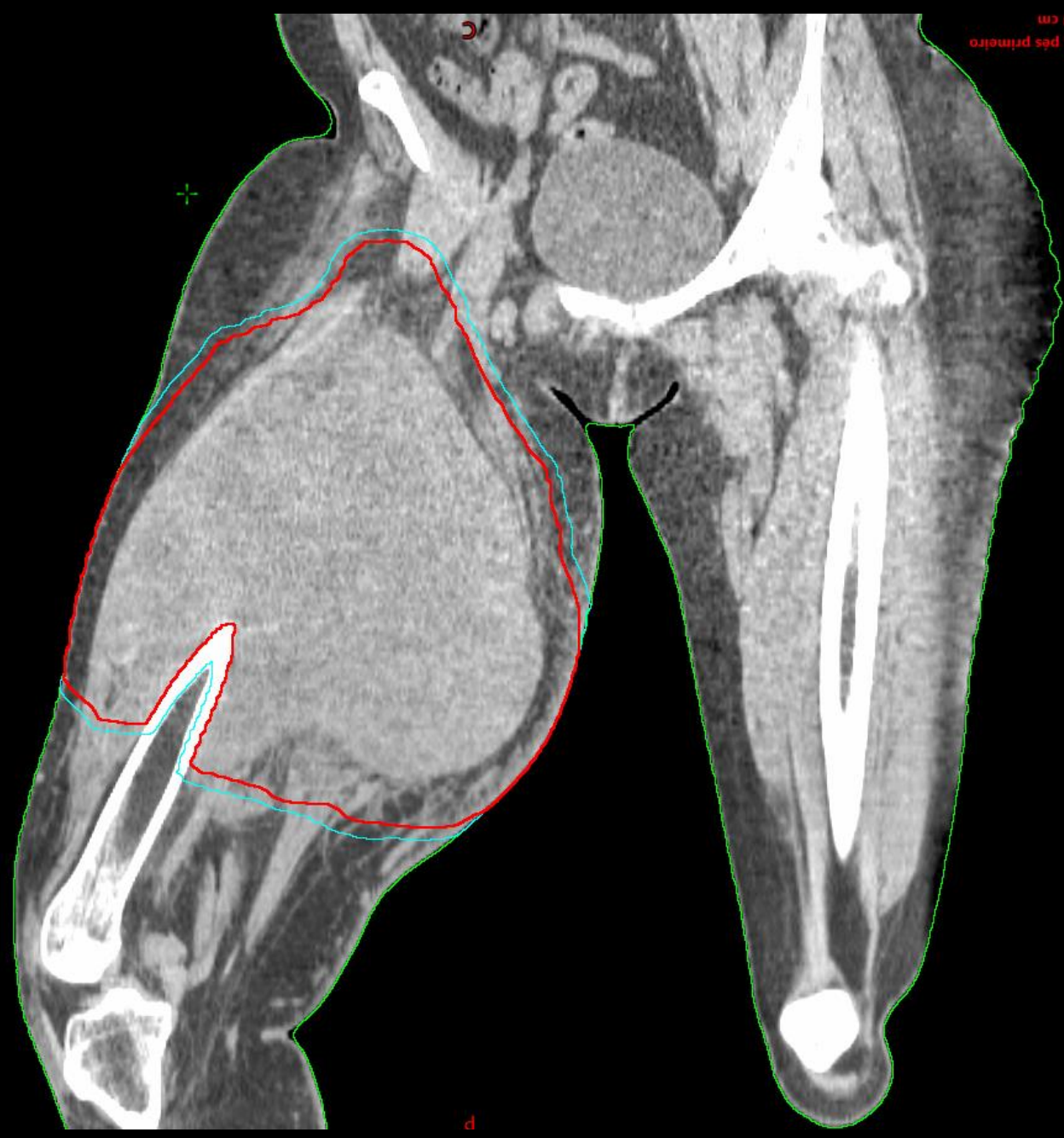
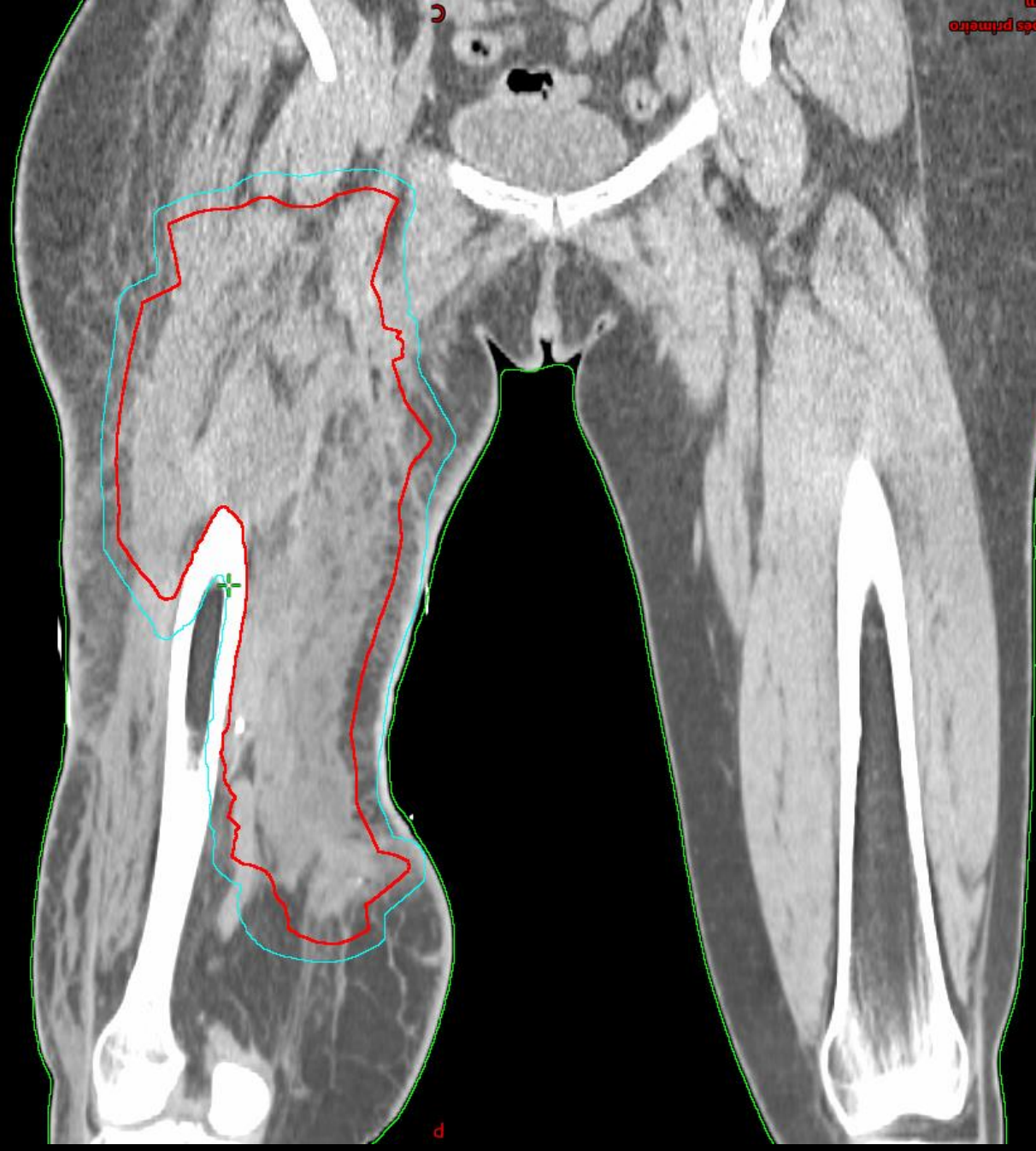
Volumes de tratamento



50Gy

60-66Gy
2 fases

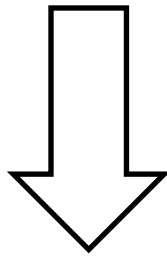




Como evoluir?

RT PRÉ - OPERATÓRIA

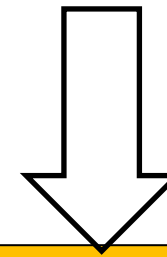
- Dose menor
- Volume menor
- ↑ Complicação FO



- 1) IMRT
- 2) IGRT
- 3) Hipofracionamento
- 4) Intensificação do tratamento

RT PÓS- OPERATÓRIA

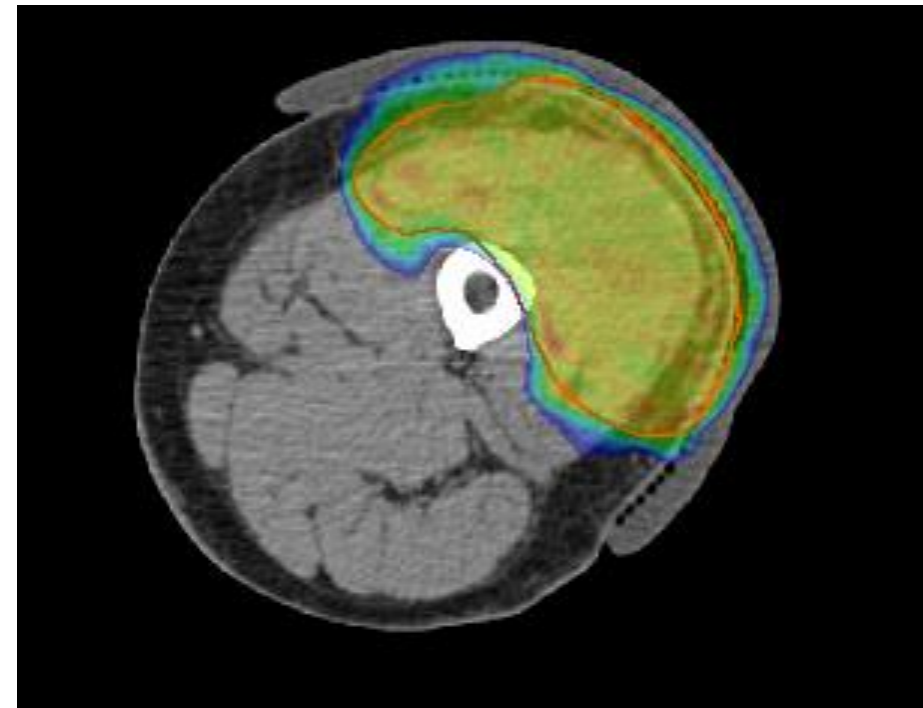
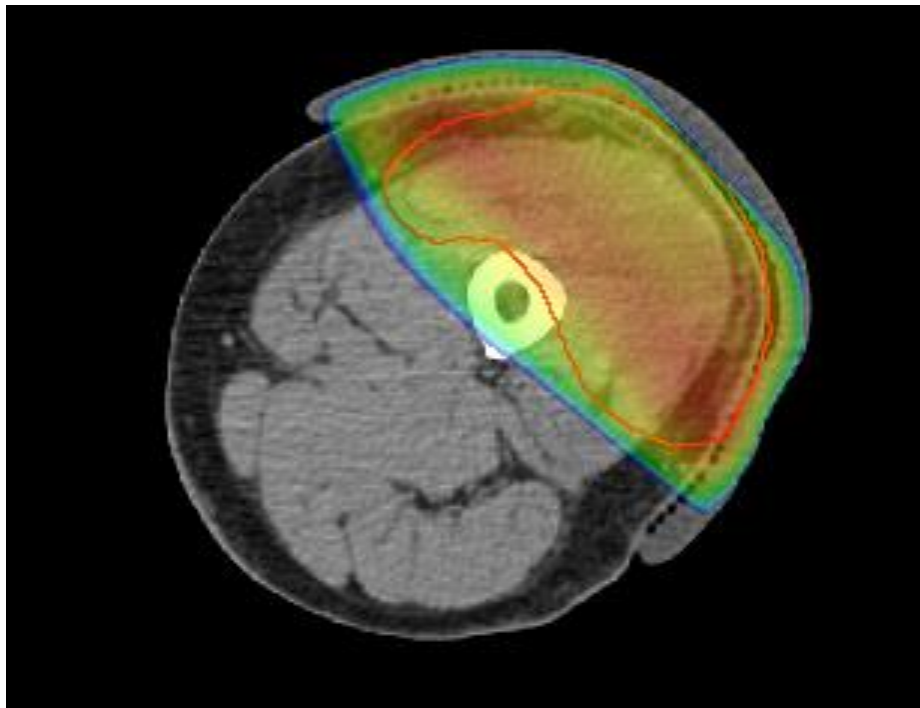
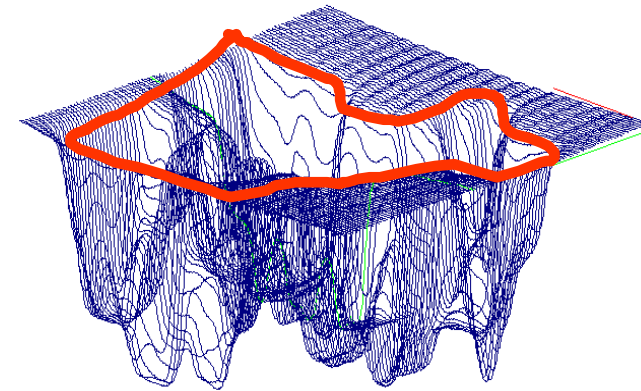
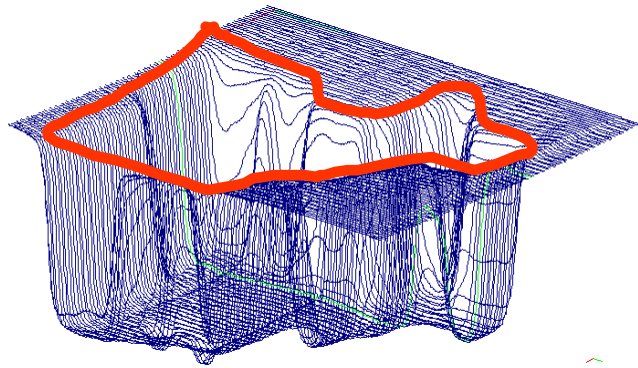
- Dose maior
- Volume maior
- ↑ Fibrose



- 1) IMRT
- 2) IGRT
- 3) Diminuir o volume de tratamento



IMRT



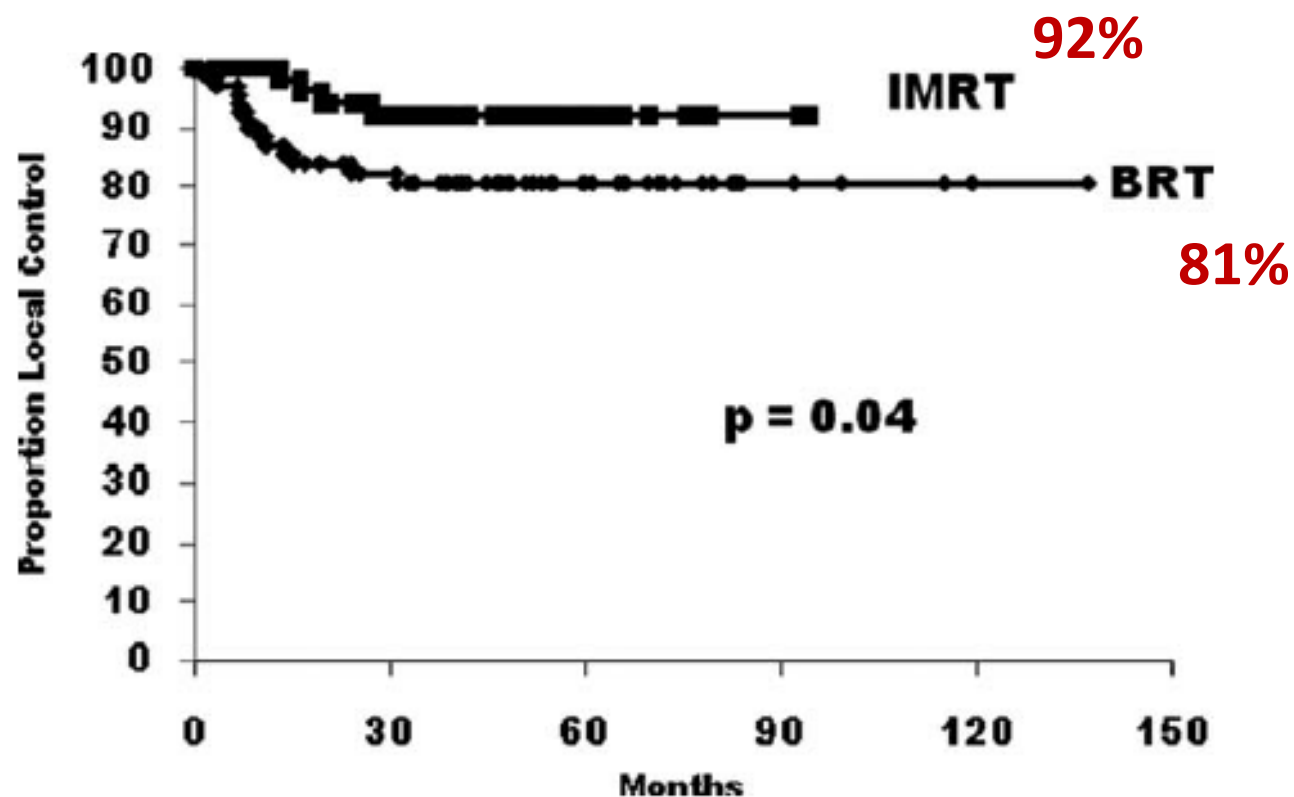
Local Control Comparison of Adjuvant Brachytherapy to Intensity-Modulated Radiotherapy in Primary High-Grade Sarcoma of the Extremity



Memorial Sloan-Kettering
Cancer Center

Kaled M. Alektiar, MD¹; Murray F. Brennan, MD²; and Samuel Singer, MD²

134 pacientes – Sarcoma de ALTO GRAU

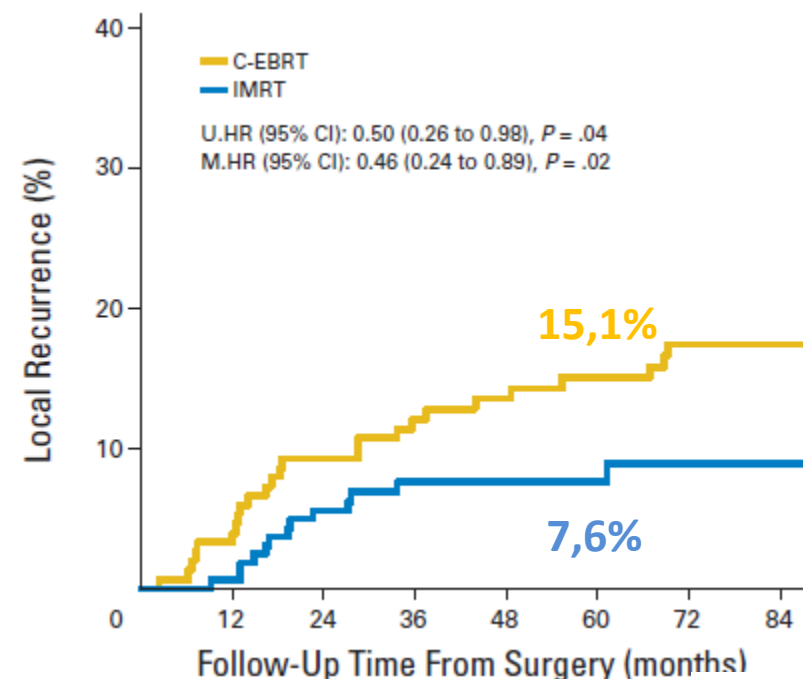


Comparison of Local Recurrence With Conventional and Intensity-Modulated Radiation Therapy for Primary Soft-Tissue Sarcomas of the Extremity

Michael R. Folkert, Samuel Singer, Murray F. Brennan, Deborah Kuk, Li-Xuan Qin, Wendy K. Kobayashi, Aimee M. Crago, and Kaled M. Alektiar

316 pacientes consecutivos

Toxicity	Overall		Conventional RT		IMRT		P
	No.	%	No.	%	No.	%	
Wound complications							
Noninfected	28	8.8	14	9.1	14	8.5	1.0
Infected	30	9.4	13	8.4	17	10.3	.70
Radiation dermatitis	127	39.8	75	48.7	52	31.5	.002
Fracture	22	6.9	14	9.1	8	4.8	.18
Nerve damage*	7	2.6	2	1.6	5	3.5	.45
Joint stiffness	41	12.9	17	11	24	14.5	.40
Edema	36	11.3	23	14.9	13	7.9	.05



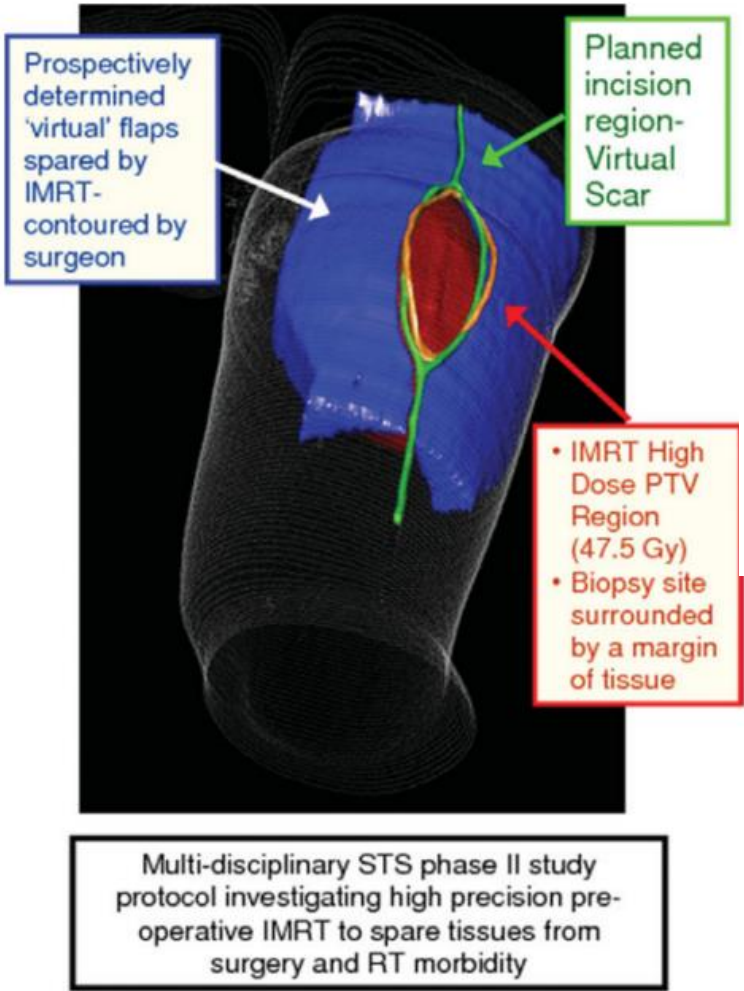


IGRT

CONE BEAM CT



Phase 2 Study of Preoperative Image-Guided Intensity-Modulated Radiation Therapy to Reduce Wound and Combined Modality Morbidities in Lower Extremity Soft Tissue Sarcoma

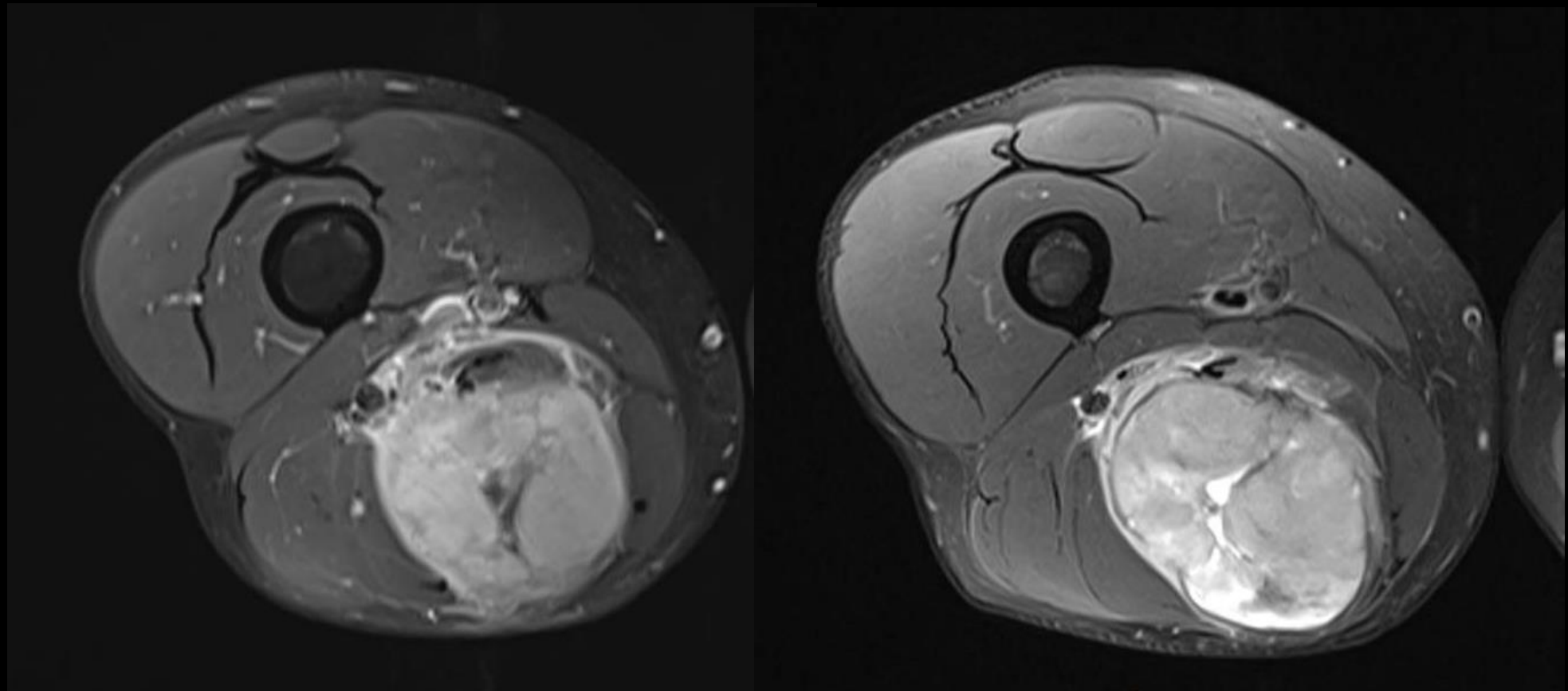


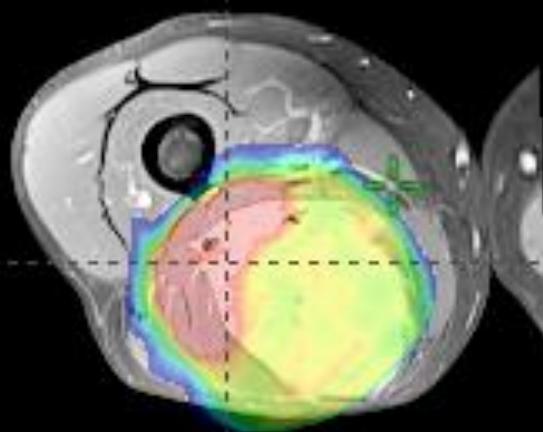
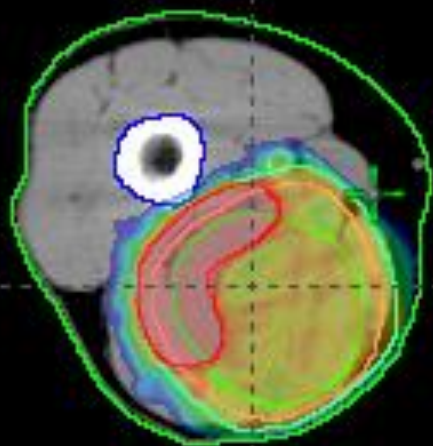
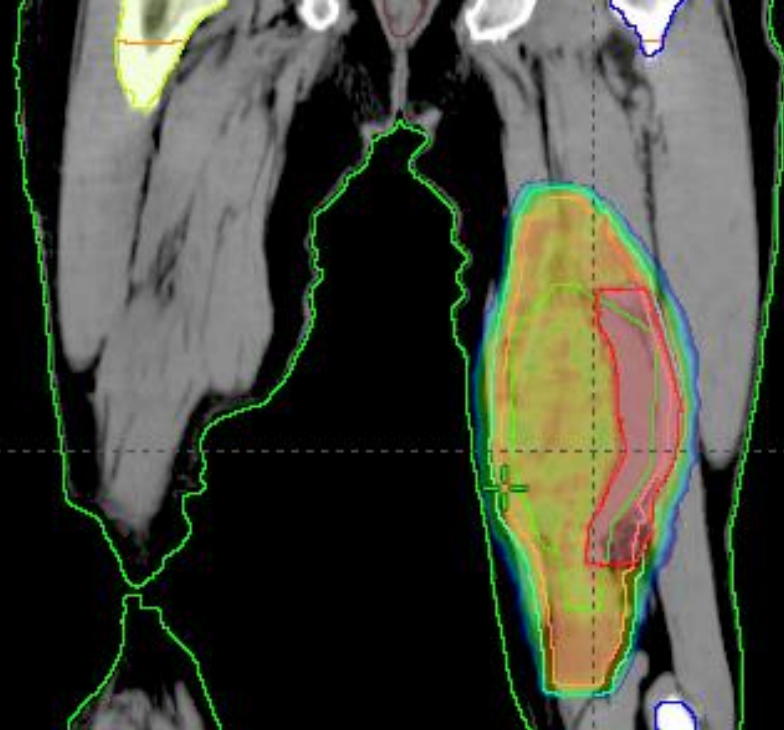
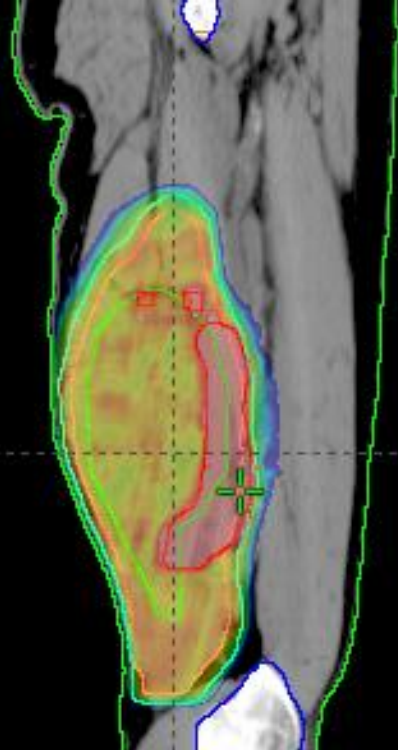
	Noncomplication	Complication	P
Mean dose to flaps	32.4 Gy	34.3 Gy	.097
Mean volume of flaps	218.5 cm ³	328.3 cm ³	.005
Mean flap width	1.69 cm	2.01 cm	.040
Mean flap thickness	1.74 cm	2.0 cm	.235
Mean flap length	25.3 cm	27.0 cm	.202
Flap and PTV overlap	21.53 cm ³	67.13 cm ³	.003
% Flap treated ≥ 30 Gy	62.7%	69.8%	.043
Mean GTV volume	608.2 cm ³	849.6 cm ³	.302
Mean CTV volume	1178.0 cm ³	1832.0 cm ³	.020

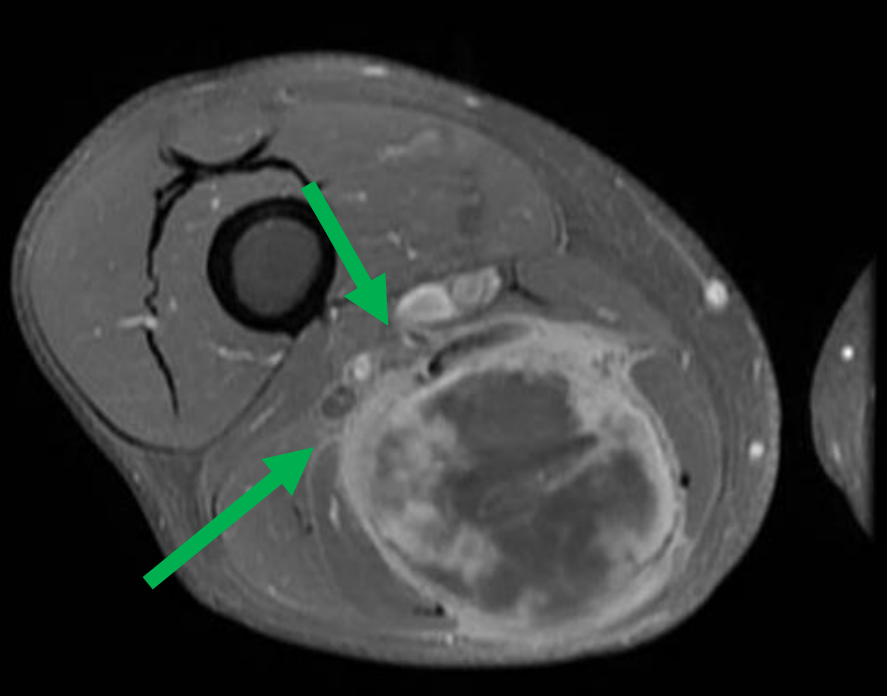
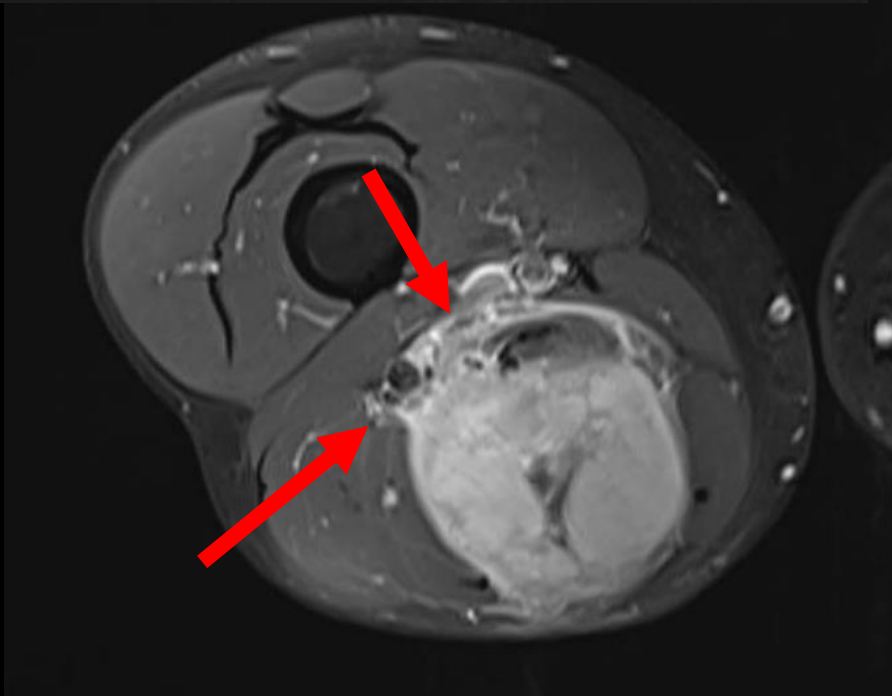
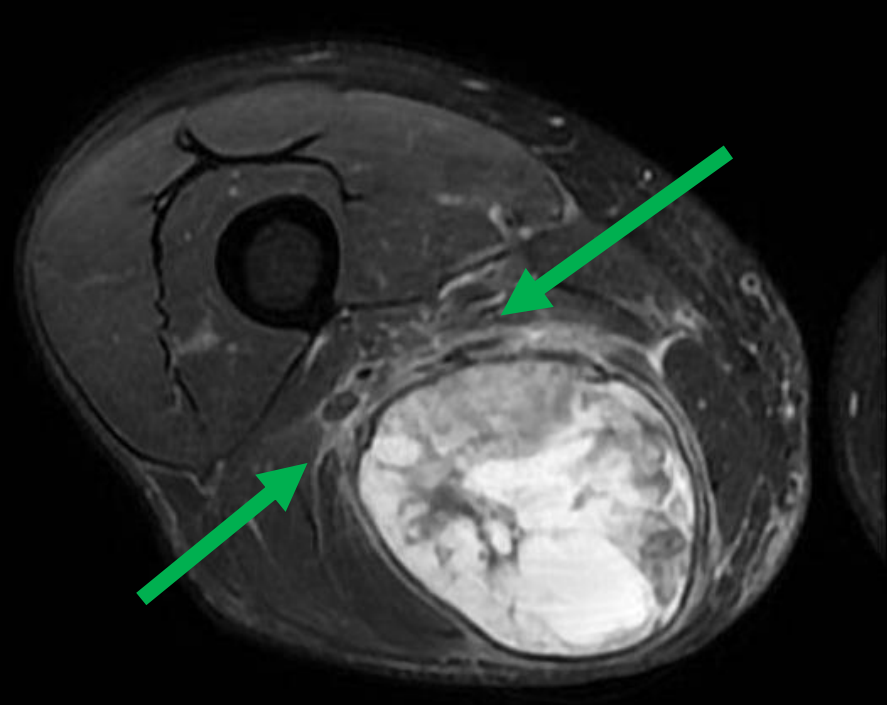
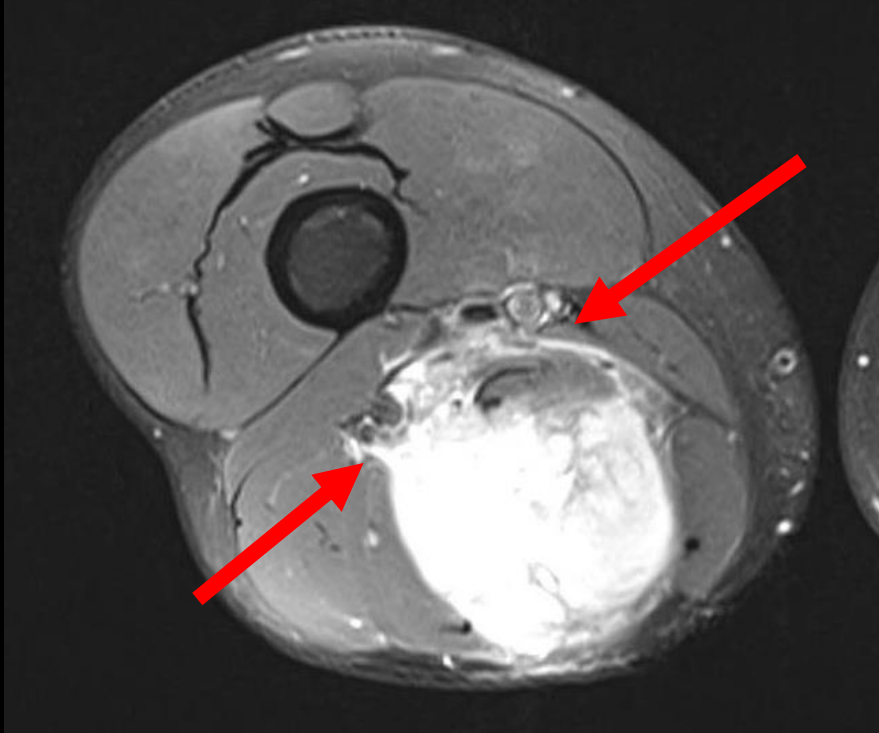
Complicações de F.O.	30,5%	(43%)*
Fechamento primário	93,2%	(71,4%)*

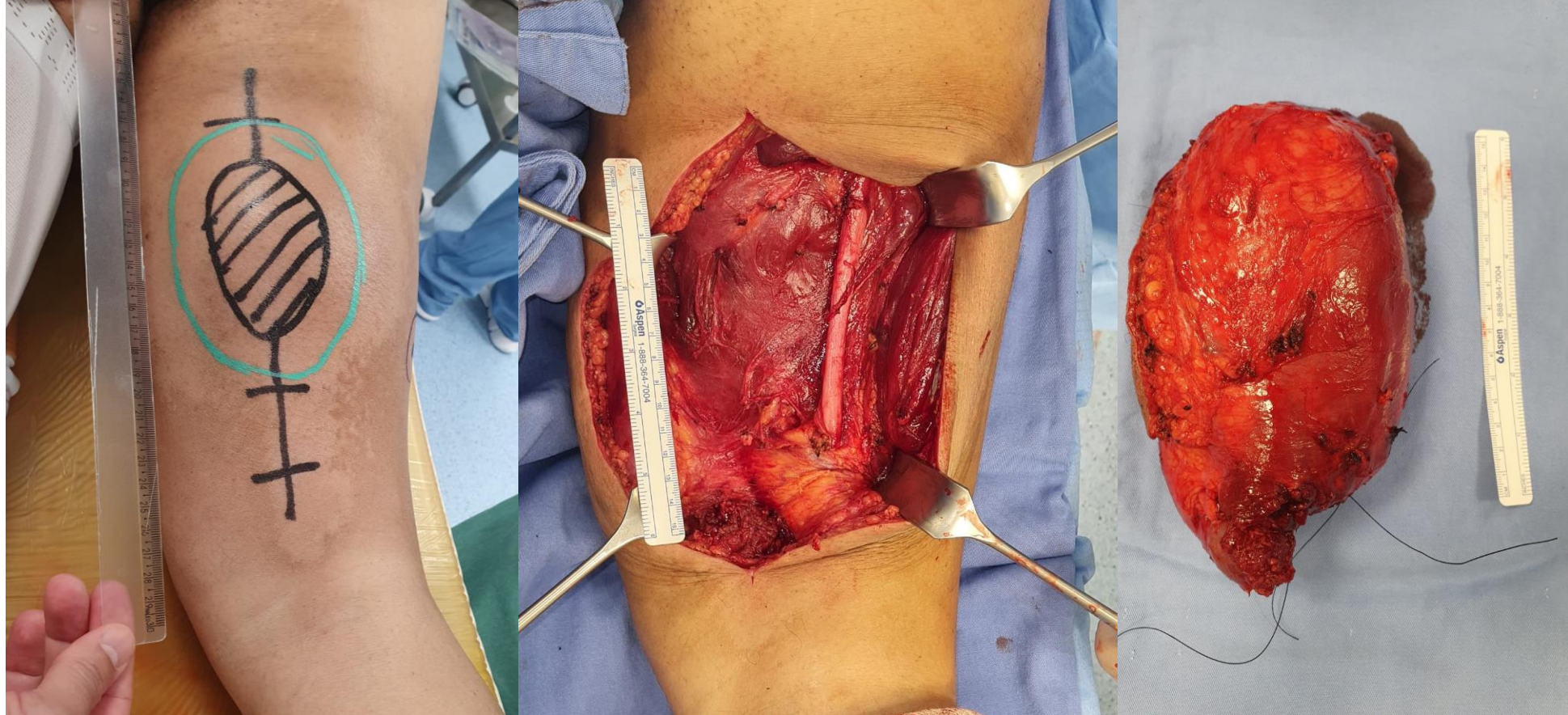


♂, 76 anos, Sarcoma pleomórfico de alto grau, coxa D 11,6 cm





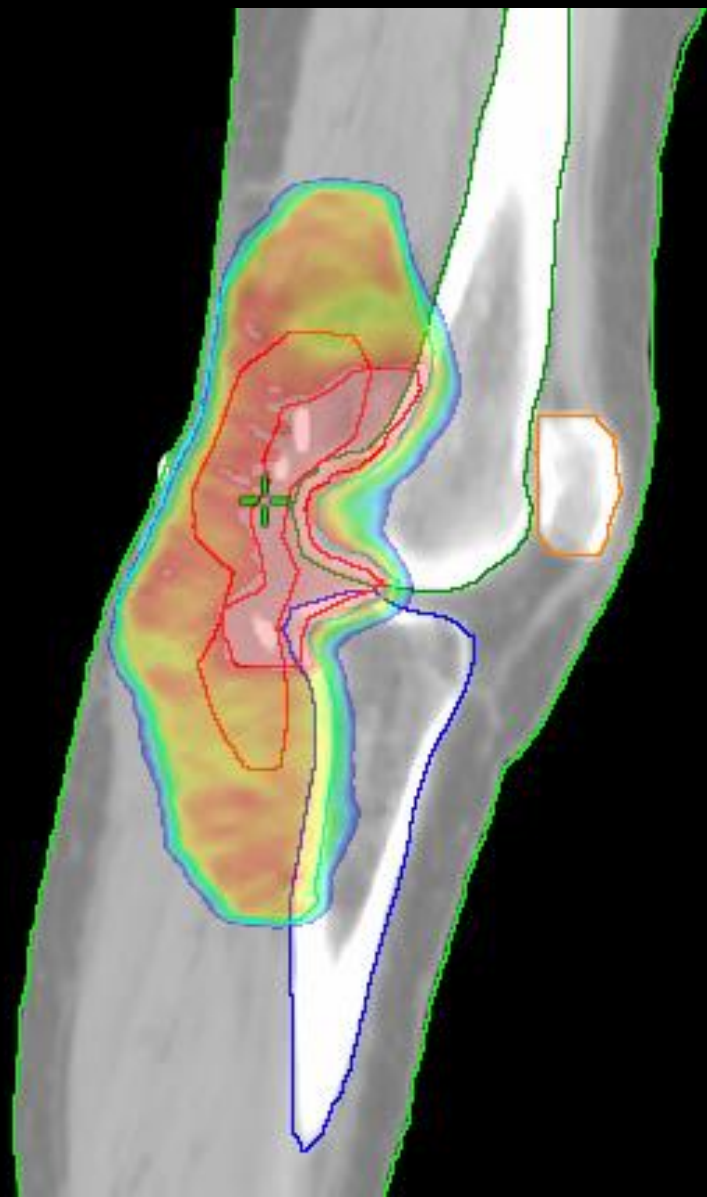
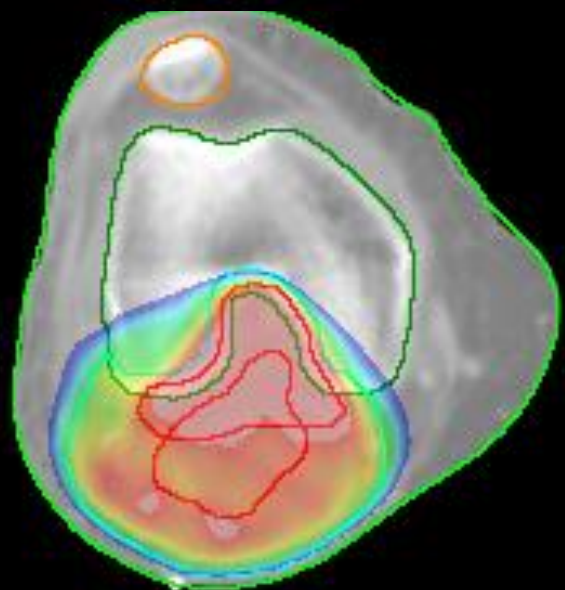
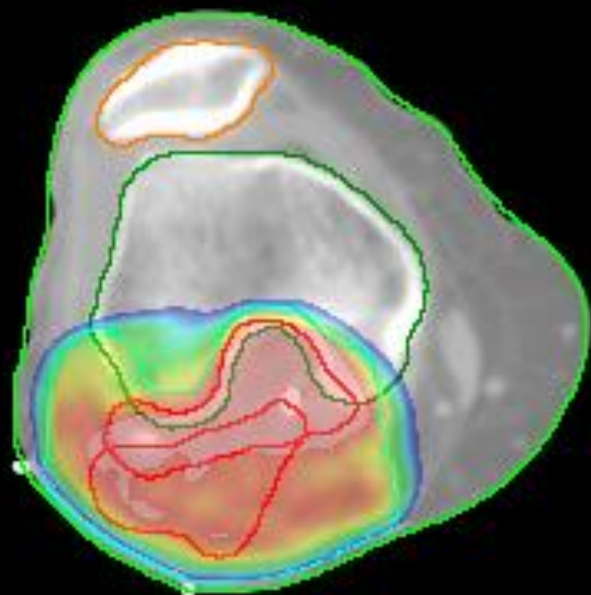
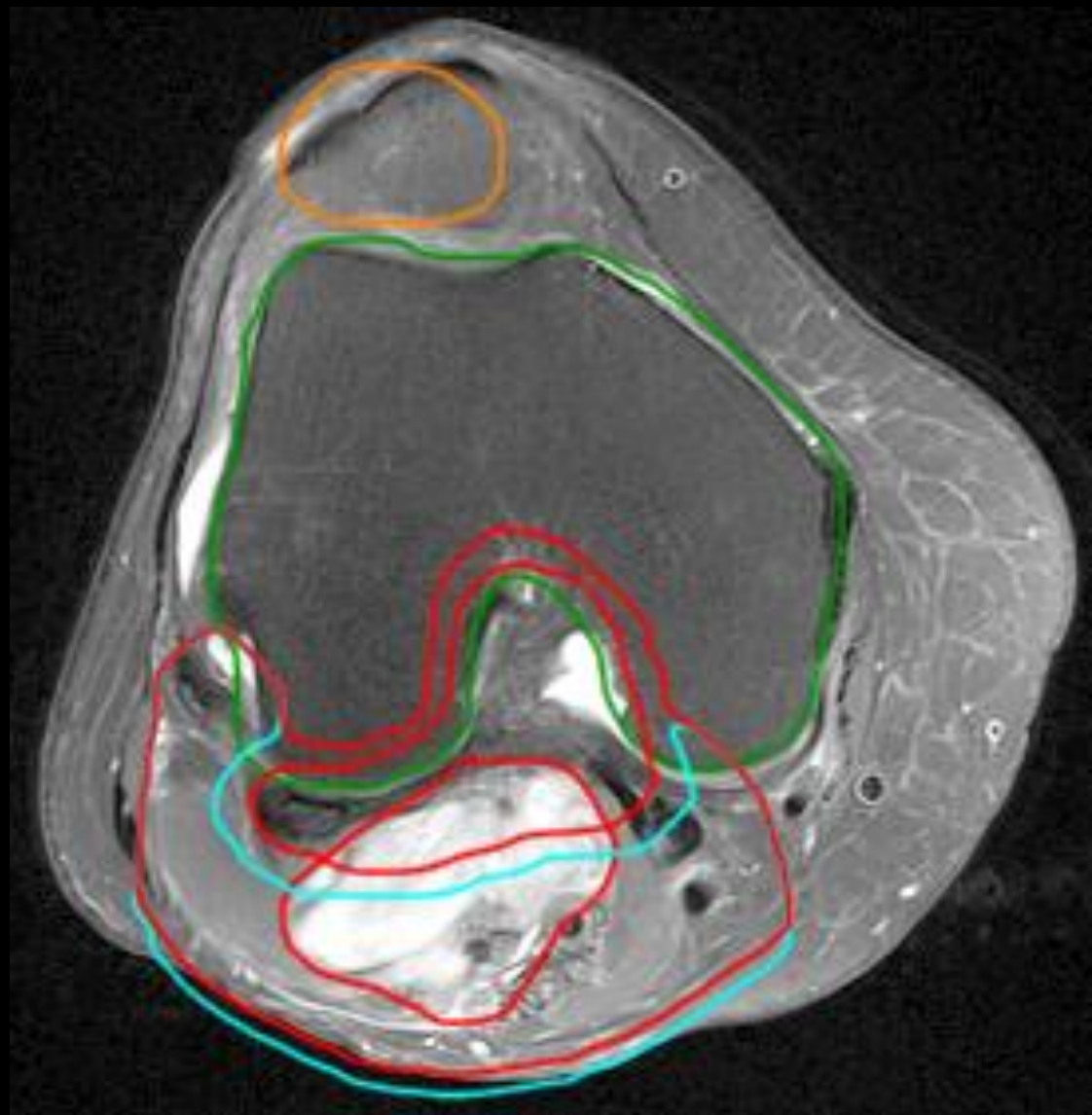




AP: Sarcoma pleomórfico de alto grau
Margens livres
85% de alterações regressivas



♀, 59 anos, Sarcoma fibromixóide de baixo grau, fossa poplítea E 11 cm



Calendário

Padrão - ICESP: 25 x 200 cGy

Mon	Tue	Wed	Thu	Fri	Sat	Sun
X	X	X	X	X		
X	X	X	X	X		
X	X	X	X	X		
X	X	X	X	X		
X	X	X	X	X		

5 semanas



Calendário

Padrão - ICESP: 30 x 200 cGy

Mon	Tue	Wed	Thu	Fri	Sat	Sun
X	X	X	X	X		
X	X	X	X	X		
X	X	X	X	X		
X	X	X	X	X		
X	X	X	X	X		
X	X	X	X	X		

6 semanas



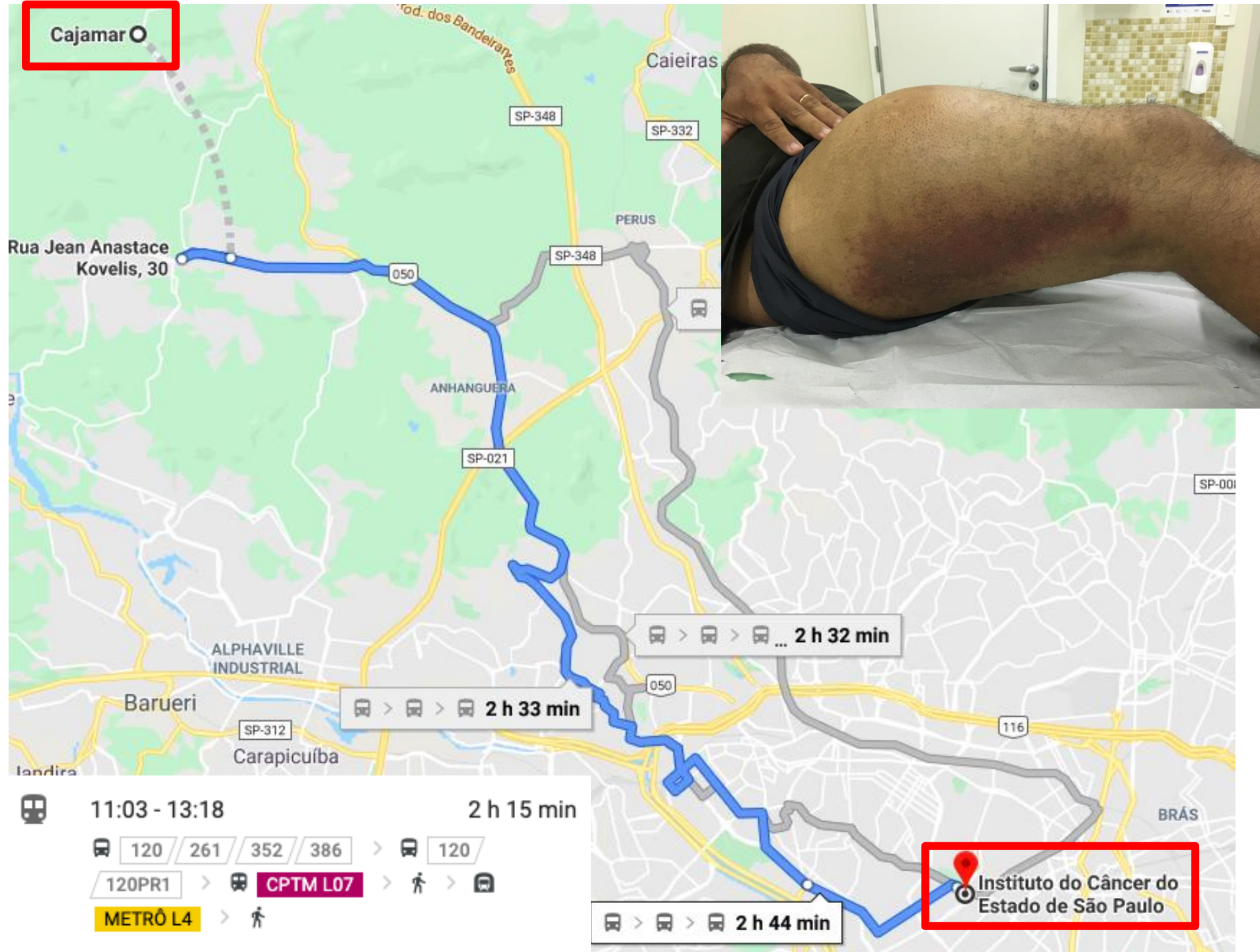
Calendário

Padrão - ICESP: 33 x 200 cGy

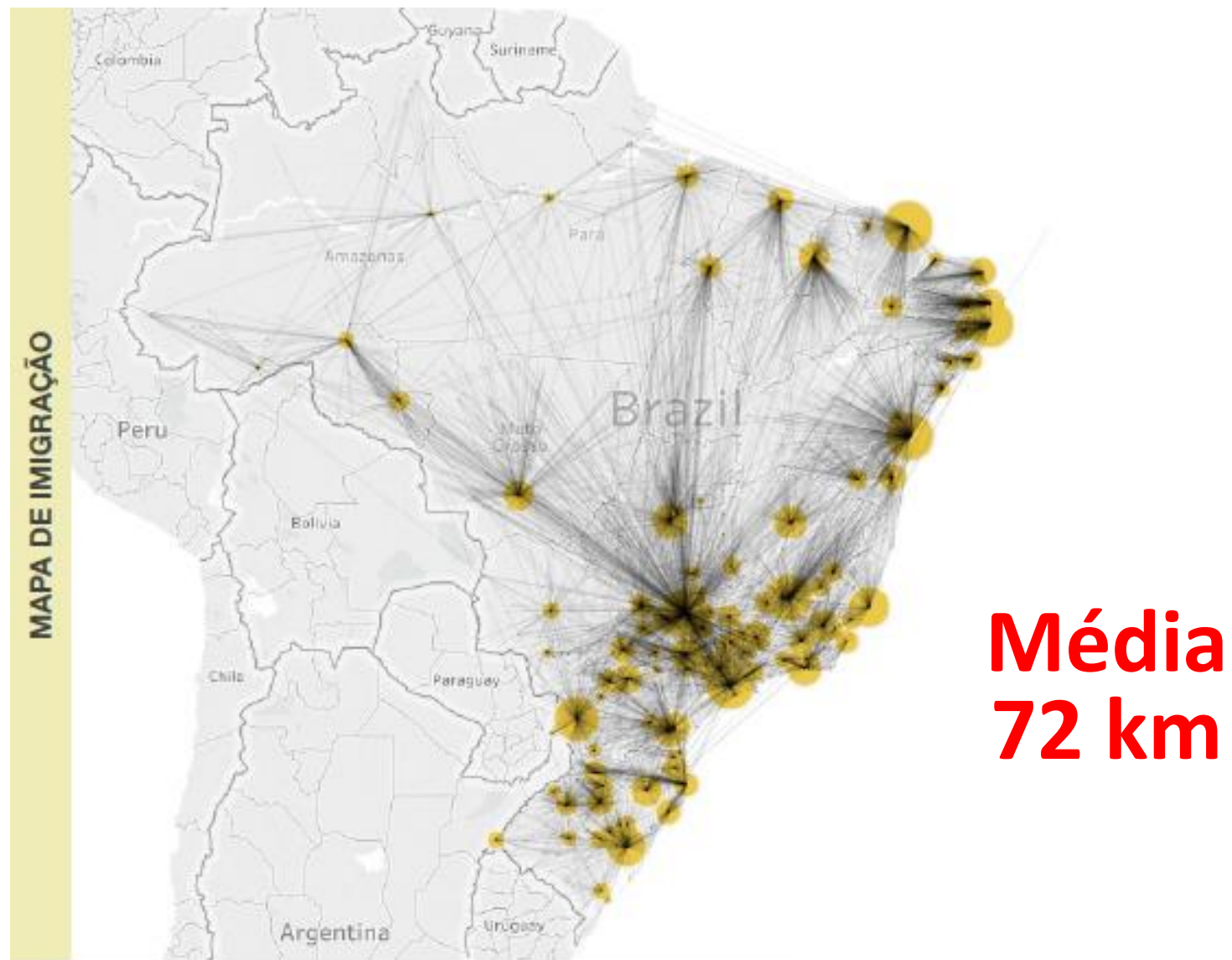
Mon	Tue	Wed	Thu	Fri	Sat	Sun
X	X	X	X	X		
X	X	X	X	X		
X	X	X	X	X		
X	X	X	X	X		
X	X	X	X	X		
X	X	X				

6,5 semanas





Realidade brasileira



Hipofracionamento em STS

TABLE 5. Selected Series of Patients Treated With Hypofractionated Radiotherapy for Soft Tissue Sarcoma

Series	No. Patients	Dose	Chemotherapy	LC
Eilber et al ¹	496	3.5 Gy×8	Yes	89% at 5 y
Mack et al ²³	75 (67 R0, 8 R1)	3.0 Gy×10	Yes	R0: 97% at 5 y R1: 50% at 5 y
Temple et al ²⁴	53 upper limb only	3.0 Gy×10	Yes	96% at 5 y
Ryan et al ²⁵	25	3.5 Gy×8	Yes, dose-intense epirubicin and ifosfamide	88% at 2 y
Jacinto et al ²⁶	49	Median 2.5 Gy×12	76% received chemotherapy	81% at 5 y
MacDermid et al ²⁷	34	3.5 Gy×8	Yes	89.0% at 5 y
Soyfer et al ²⁸	21 elderly patients	3.0 Gy×13-16	No	86% at 26 mo
Koseła-Paterczyk et al ²⁹	272 (167 with primary tumors)	5 Gy×5	Yes in 81%, for “more chemosensitive subtypes (eg, synovial sarcoma)”	81% at 3 y
Kubicek et al ³⁰	13 patients, 14 tumors	SBRT: 7 Gy×5 for 12 patients; 8 Gy×5 for 2 deeper tumors	3 patients had chemo before SBRT	1 local failure at 488 d. Median follow-up, 279 d



Dose equivalente dos estudos

TABLE 5. Selected Series of Patients Treated With Hypofractionated Radiotherapy for Soft Tissue Sarcoma

Series	No. Patients	Dose	
Eilber et al ¹	496	3.5 Gy×8	38.5 Gy
Mack et al ²³	75 (67 R0, 8 R1)	3.0 Gy×10	37.5 Gy
			37.5 Gy
Temple et al ²⁴	53 upper limb only	3.0 Gy×10	38.5 Gy
Ryan et al ²⁵	25	3.5 Gy×8	33.7 Gy
Jacinto et al ²⁶	49	Median 2.5 Gy×12	38.5 Gy
MacDermed et al ²⁷	34	3.5 Gy×8	
Soyfer et al ²⁸	21 elderly patients	3.0 Gy×13-16	36.5-45 Gy
Koseła-Paterczyk et al ²⁹	272 (167 with primary tumors)	5 Gy×5	43.7 Gy
Kubicek et al ³⁰	13 patients, 14 tumors	SBRT: 7 Gy×5 for 12 patients; 8 Gy×5 for 2 deeper tumors	78-100 Gy

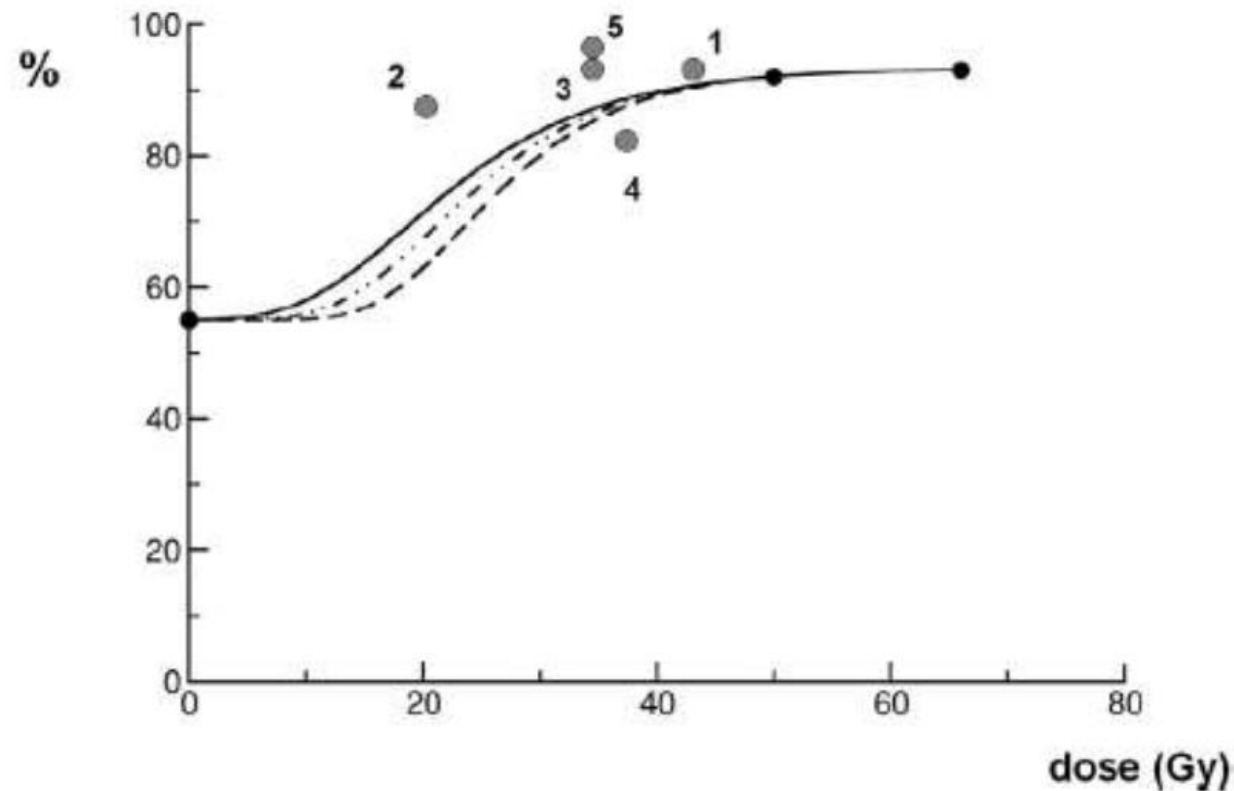


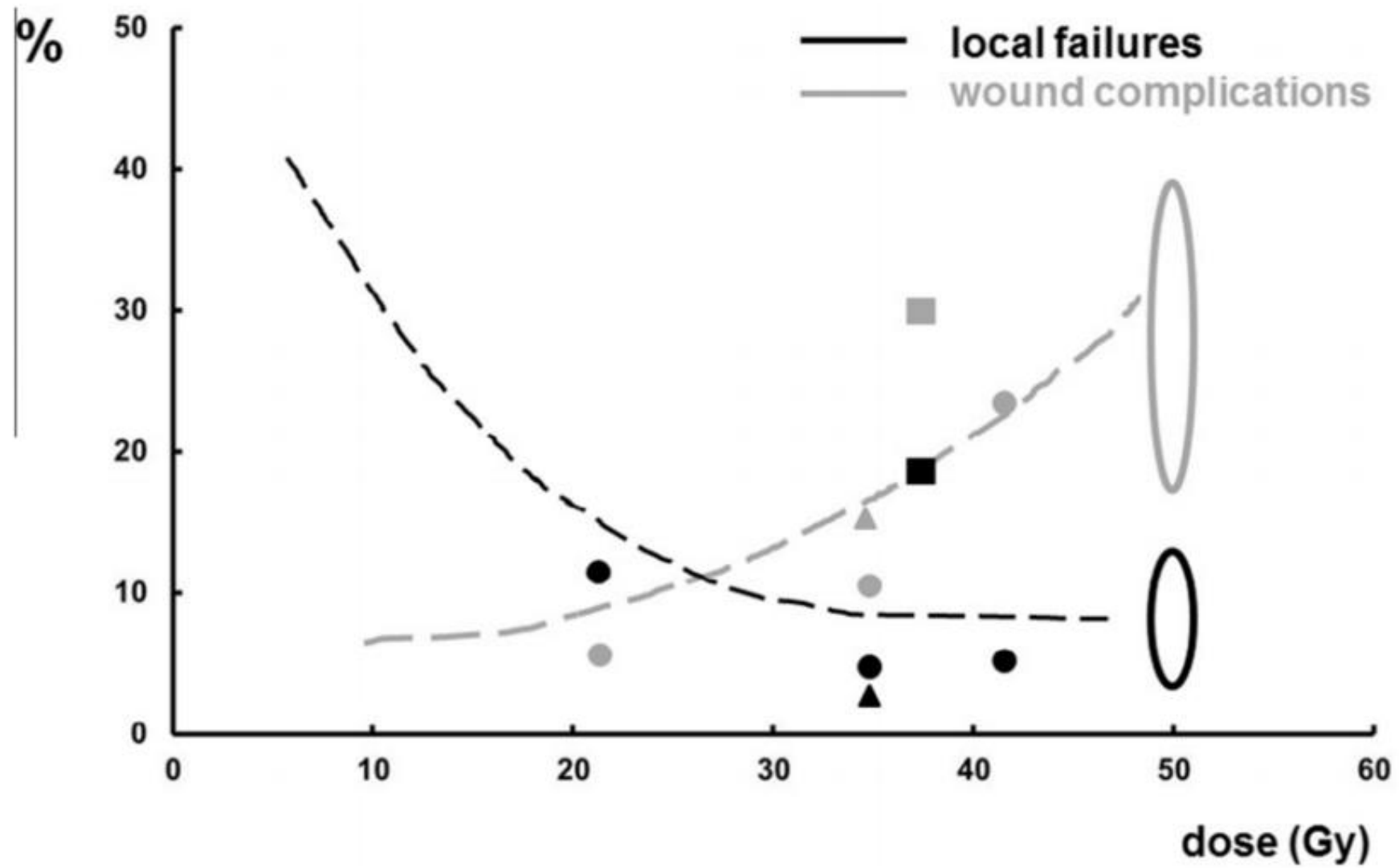
Preoperative radiotherapy for extremity soft tissue sarcoma; past, present and future perspectives on dose fractionation regimens and combined modality strategies



Rick L.M. Haas^{a,*}, Aisha B. Miah^b, Cécile LePechoux^c, Thomas F. DeLaney^d, Elizabeth H. Baldini^e, Kaled Alektiar^f, Brian O'Sullivan^g

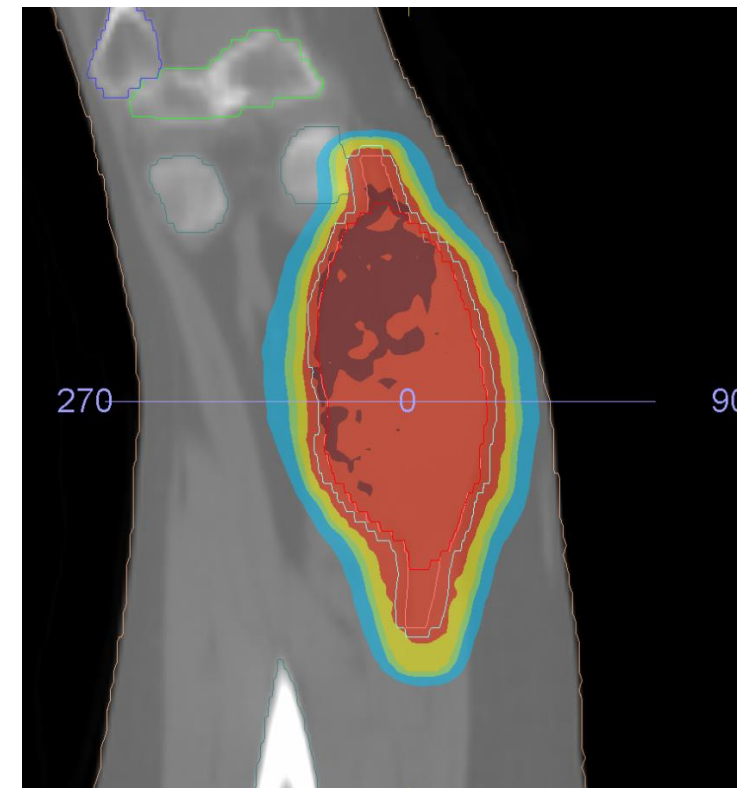
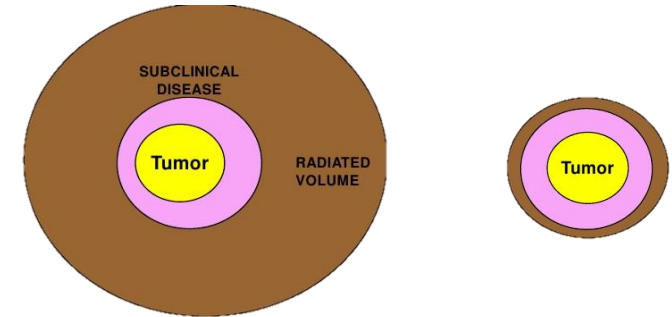
local control





SABR - Racional

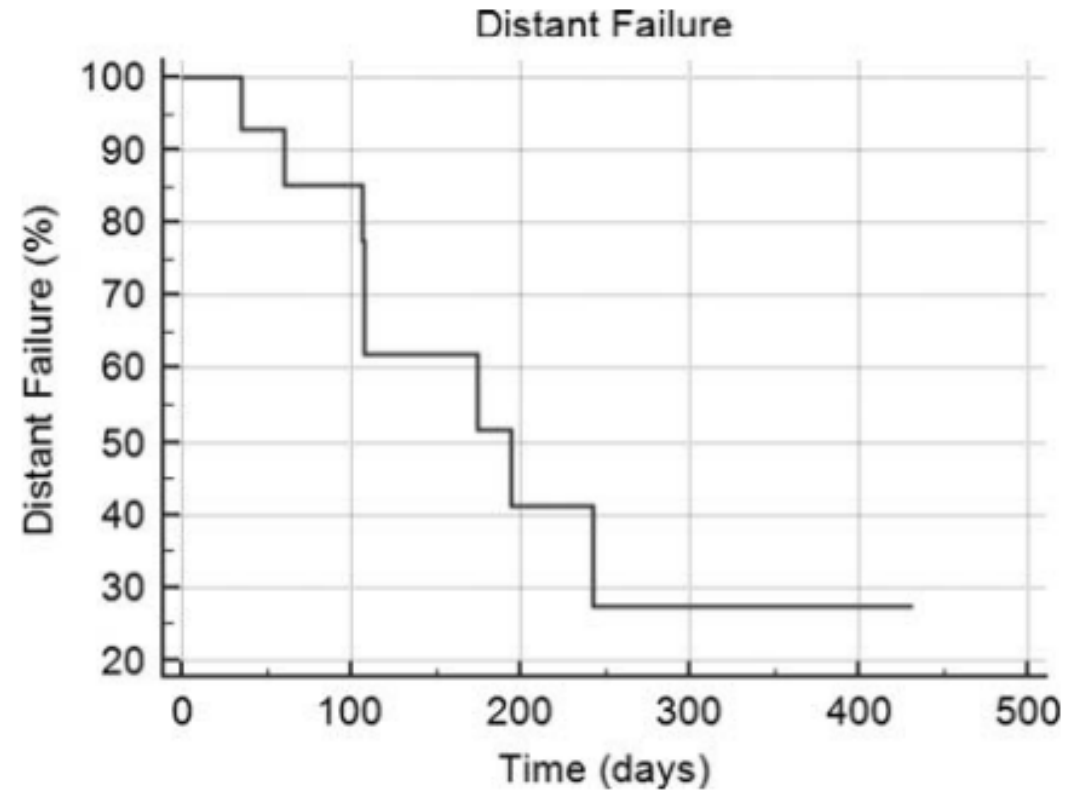
- Hipofracionamento: tendência
- Conveniência: Limitações ao deslocamento
- Coerência radiobiológica
- Radiorresistência → dose ablativa
- Conformidade → estereotaxia



SABR

Resultados MDACC

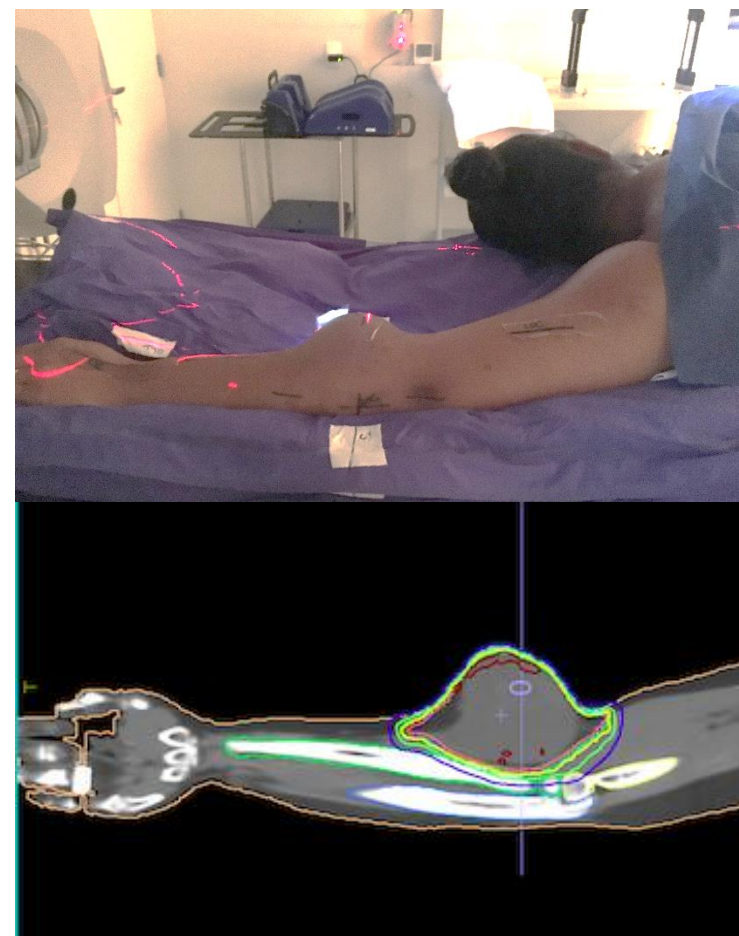
- 5x7 ou 5x8Gy
- 13 pacientes
- Tamanho mediano: 7,6cm
- Taxa mediana de necrose: 60%
- 4 complicações de F.O: 30,7%



SABR

Resultados ICESP

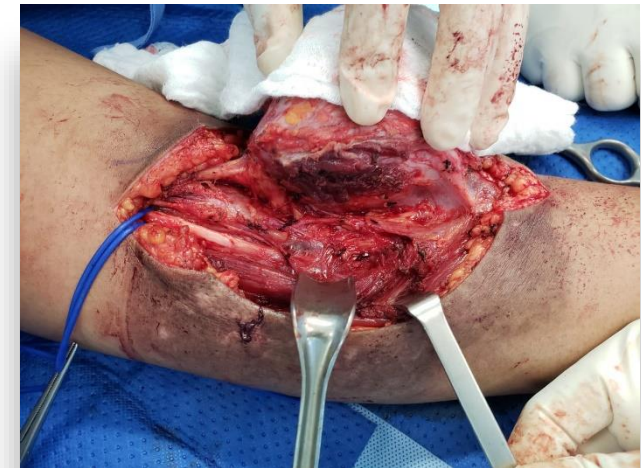
- 25 pacientes
- 5x8Gy
- CTV: GTV + 0.3 - 0.5 cm radial e 2 - 3 cm crânio-caudal. PTV: 3 mm
- Tamanho mediano: 14,5 cm
- Endpoint primário: Complicações de F.O.



SABR

Cirurgia e patologia

Reconstrução	Fechamento primário	17	68%
	Retalho	5	20%
	Enxerto	3	12%
Margem	Livre	13	52%
	Próxima	11	44%
	Positiva	1	4%
Regressão histopatológica	Média	(DP)	62,2%
	Mediana	(intervalo)	65%(0-100)



Resposta patológica completa:

$$5/24 = \mathbf{20,8\%}$$



SABR

Complicações de ferida operatória

Complicações de FO		28%
Fechamento primário		23,5%
Enxerto		40%
Retalho		50%
		p = 0,753

SABR

Toxicidade tardia



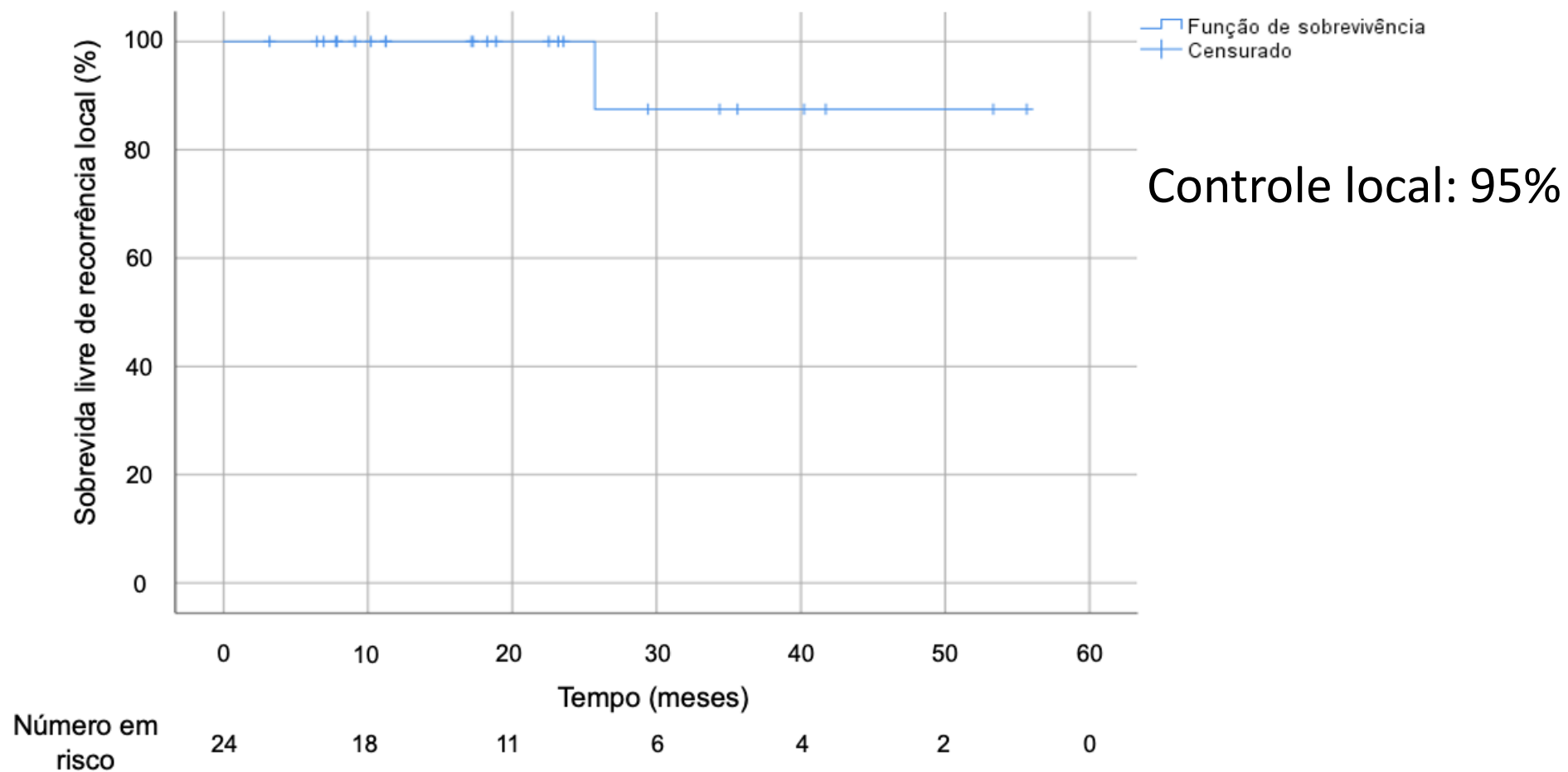
	Grau ≥ 1	Grau ≥ 2	Grau 3
Fibrose	34,7%	4,3%	-
Edema	21,7%	4,3%	-
Disfunção motora do membro	39,1%	13%	4,3%

- 1 fratura
- 4 amputações



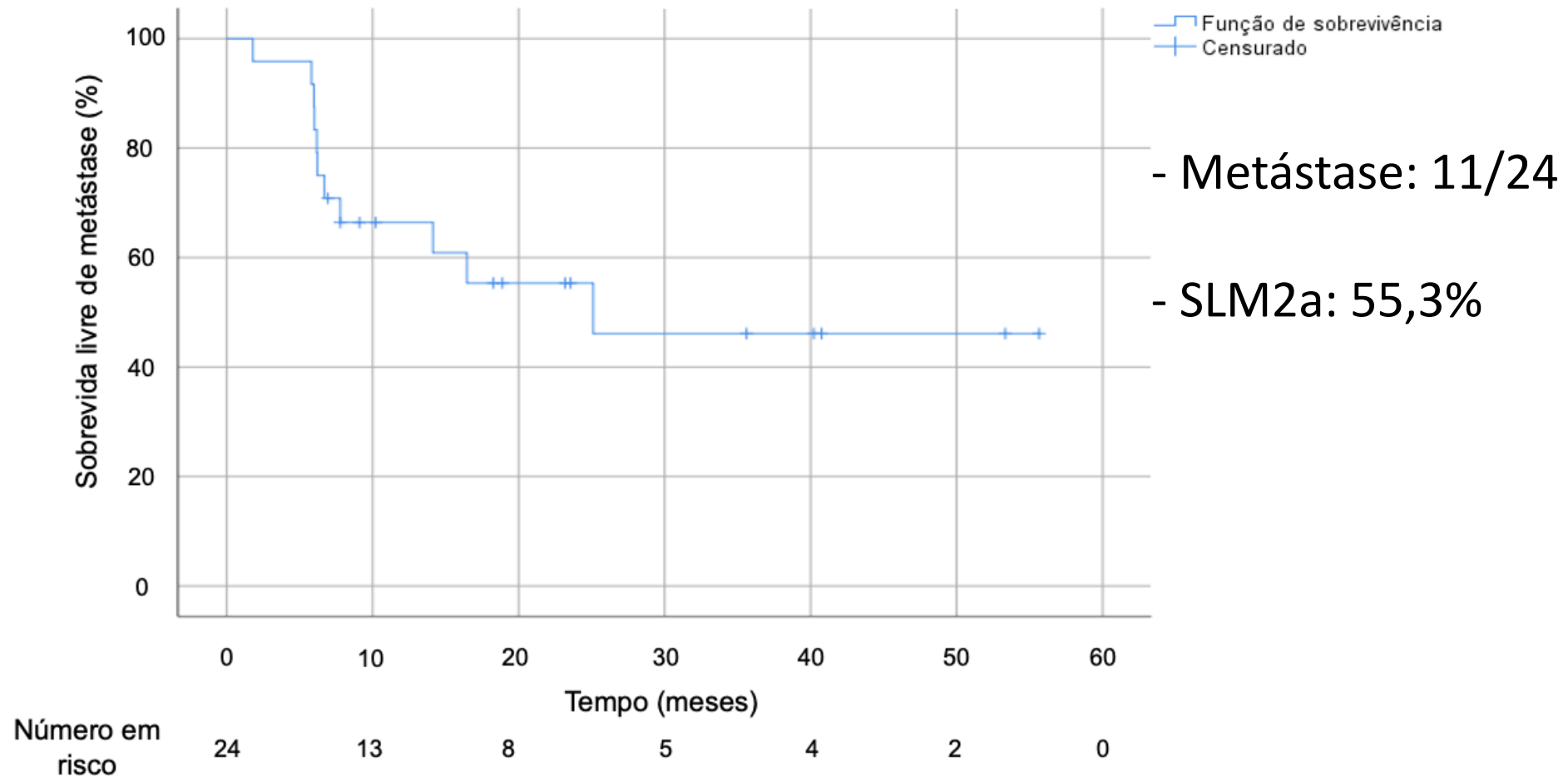
SABR

Desfechos oncológicos iniciais



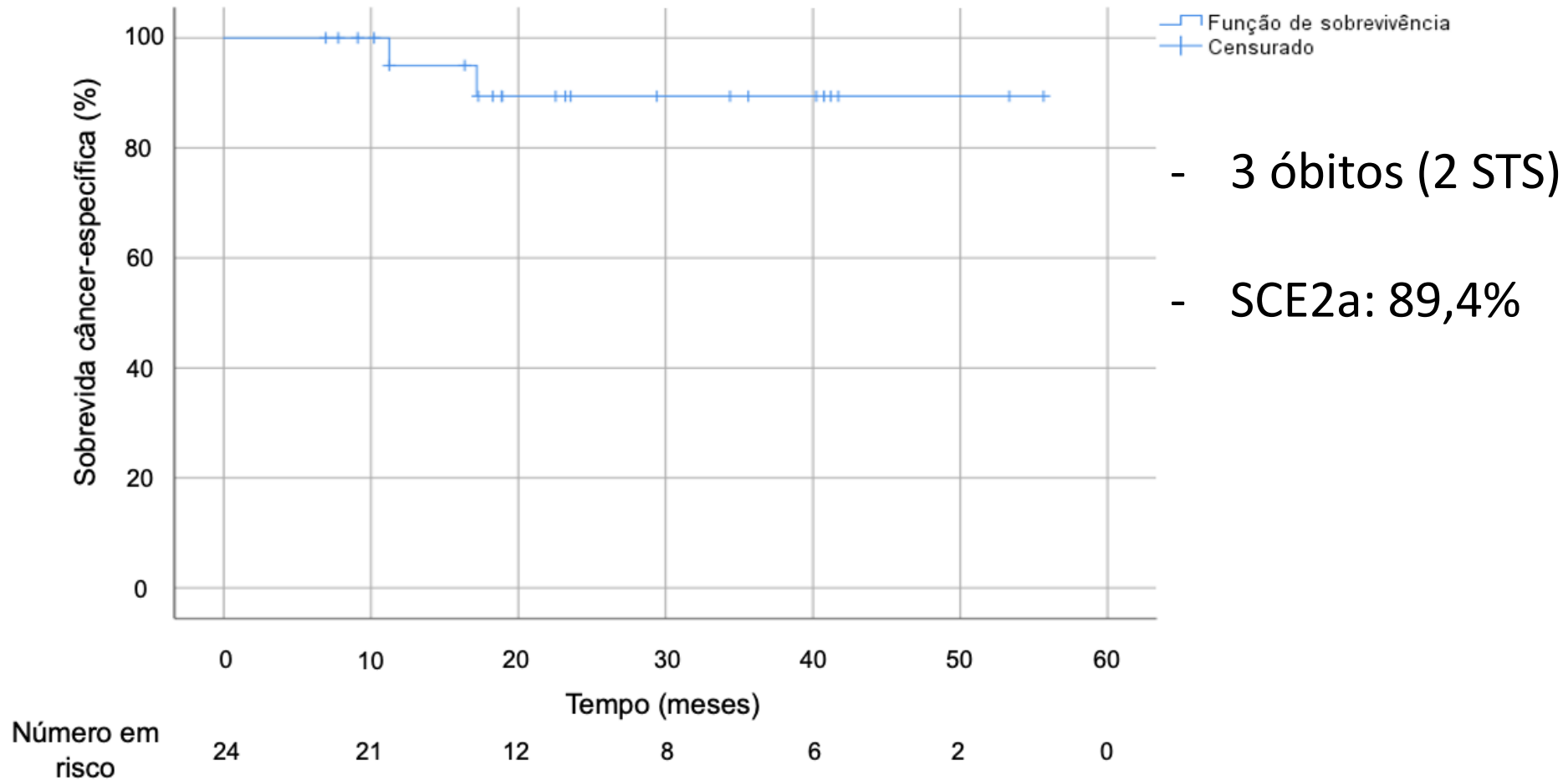
SABR

Desfechos oncológicos iniciais

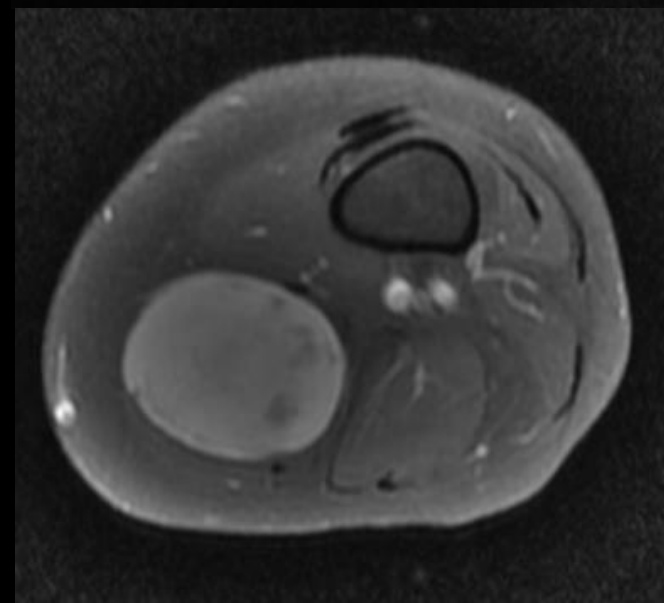
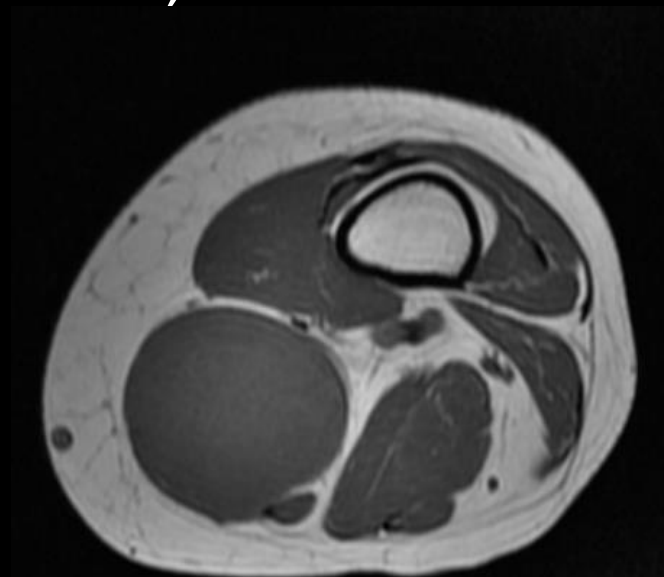
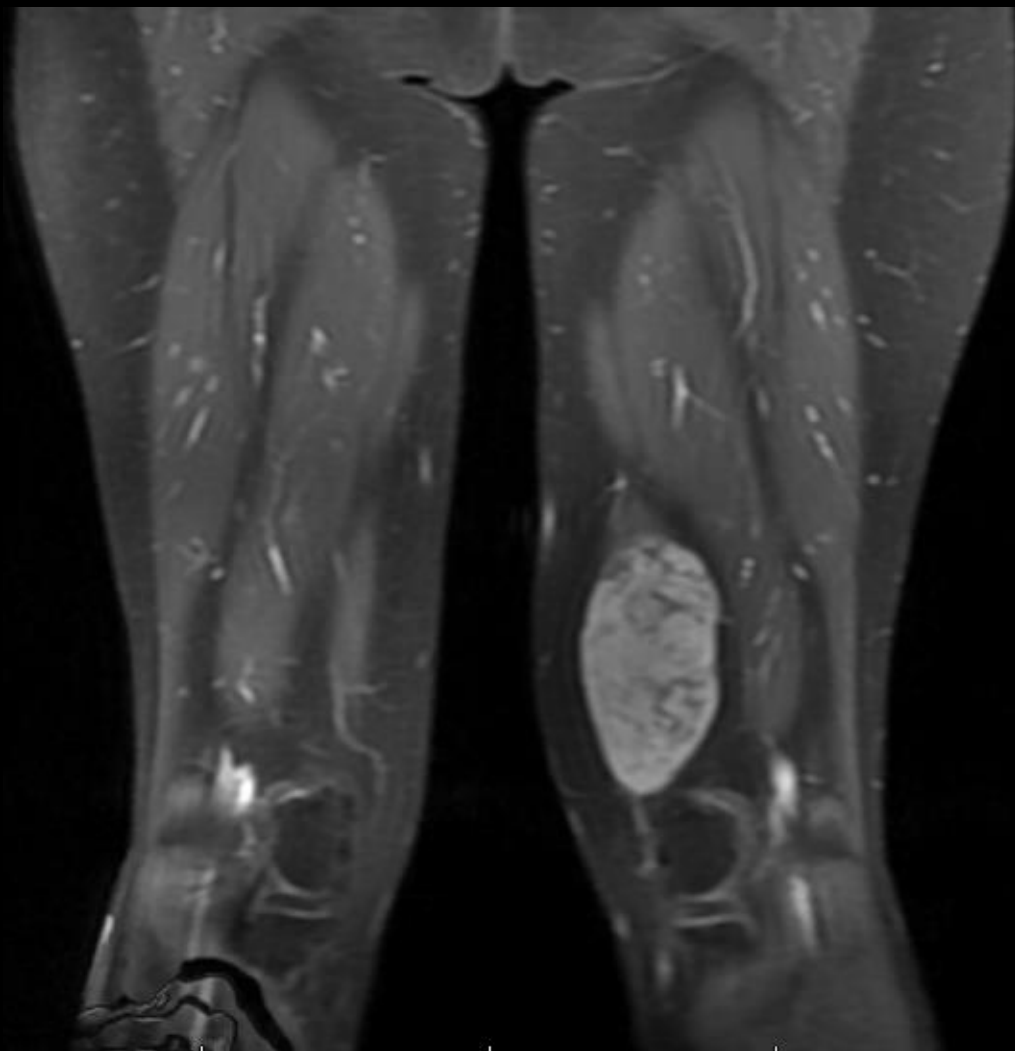


SABR

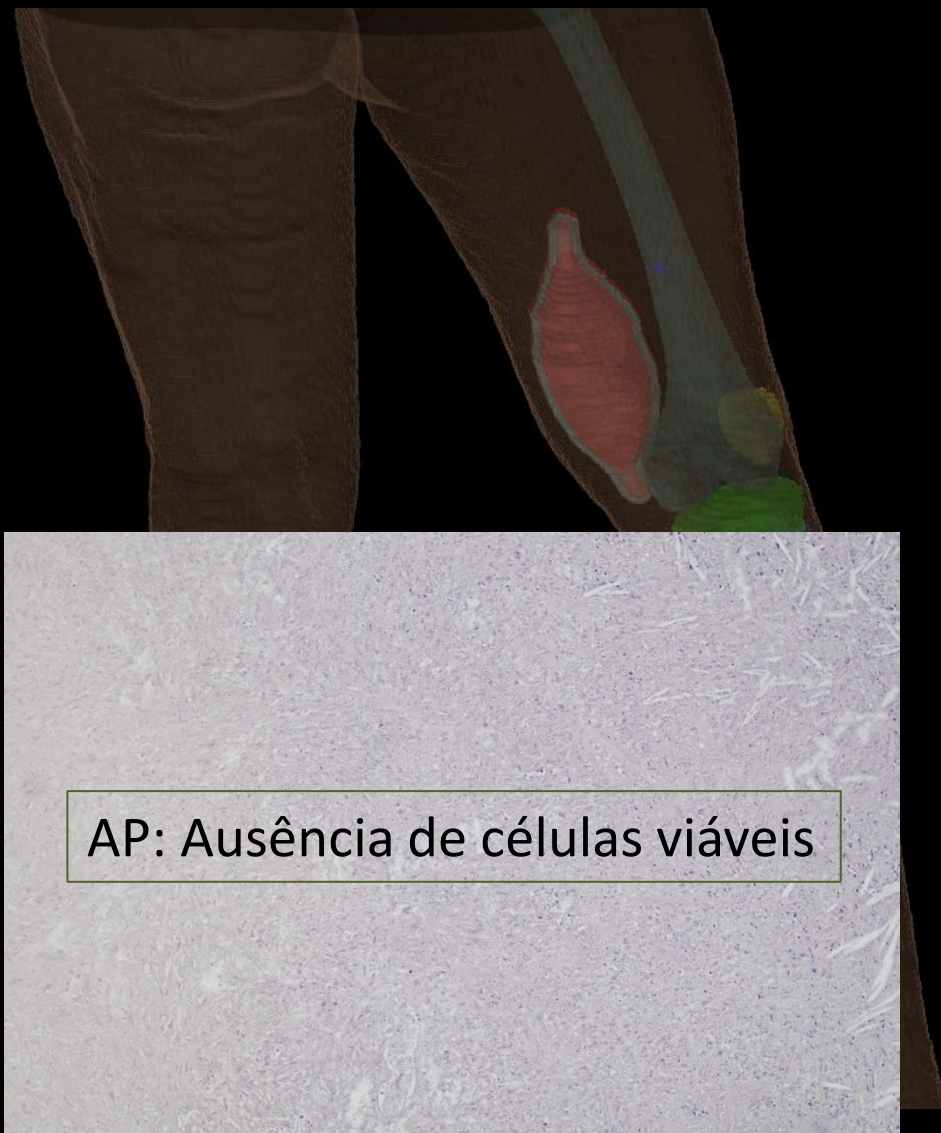
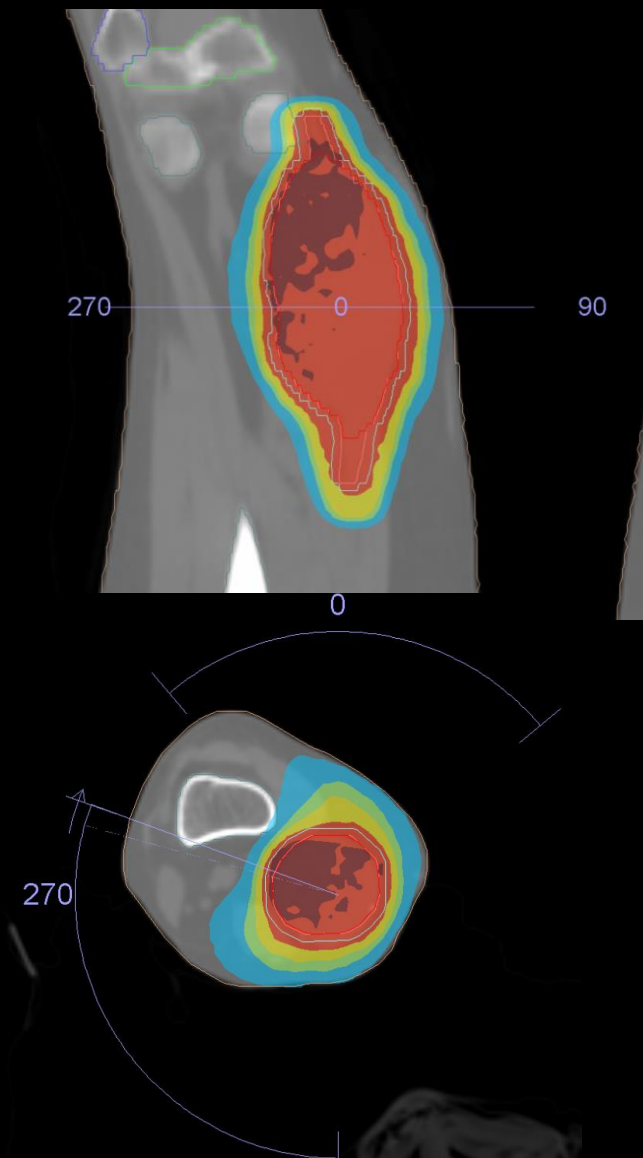
Desfechos oncológicos iniciais



♀, 37 anos, Lipossarcoma mixóide, coxa E, 10 cm



♀, 37 anos, Lipossarcoma mixóide, coxa E, 10 cm



Consenso ASTRO 2021

Practice Guideline

Radiation Therapy for Treatment of Soft Tissue Sarcoma in Adults: Executive Summary of an ASTRO Clinical Practice Guideline



Kilian E. Salerno, MD,^{a,*} Kaled M. Alektiar, MD,^b Elizabeth H. Baldini, MD, MPH,^c Manpreet Bedi, MD,^d Andrew J. Bishop, MD,^e Lisa Bradfield, BA,^f Peter Chung, MBChB,^g Thomas F. DeLaney, MD,^h Andrew Folpe, MD,ⁱ John M. Kane, III, MD,^j X. Allen Li, PhD,^k Ivy Petersen, MD,^l John Powell, MD,^m Michael Stolten, MD,ⁿ Steven Thorpe, MD,^o Jonathan C. Trent, MD, PhD,^p Maria Voermans, BS,^q and B. Ashleigh Guadagnolo, MD, MPH^r



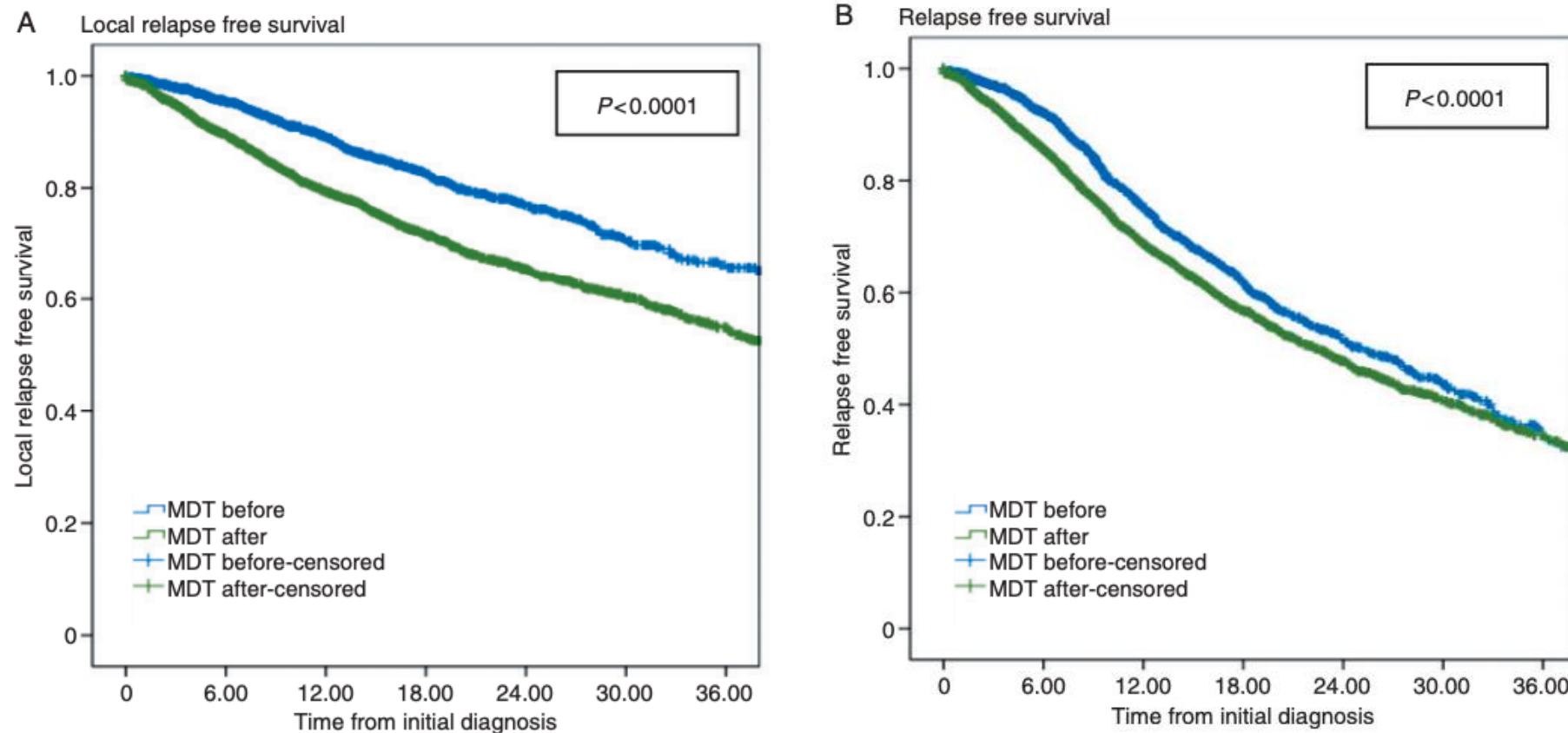
RESEARCH ARTICLE

Brazilian consensus on the diagnosis and treatment of extremities soft tissue sarcomas

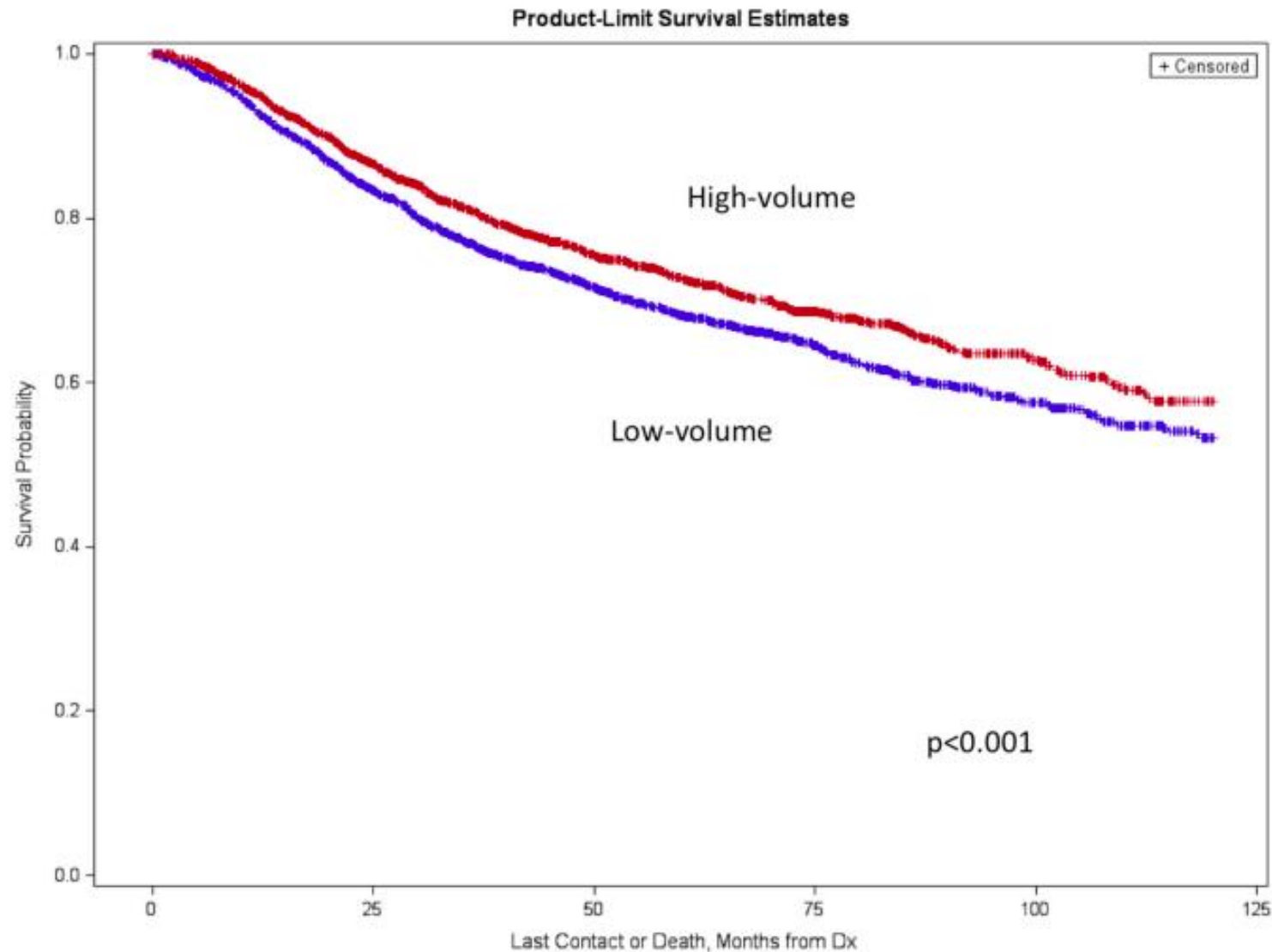
Ranyell M. S. S. B. Spencer MD, PhD¹  | Veridiana P. de Camargo MD² |
Maria L. G. Silva MD, MSc³ | Fabio F. E. Pinto MD, PhD⁴ |
Felipe D'Almeida Costa MD, PhD⁵ | Wagner S. Cequeira MD⁶ |
Rodrigo R. Munhoz MD, MSc² | Celso A. Mello MD, PhD² | Rafael A. Schmerling MD² |
Waldec J. D. Filho MD, MSc² | Tharcisio M. Coelho MD³ |
Alexandre V. A. Ambrosio MD³ | Elton T. T. Leite MD³ | Samir A. Hanna MD, PhD³  |
Sueli A. Nakagawa MD⁴ | Andre M. Baptista MD, PhD⁴ |
Rodrigo N. Pinheiro MD, MSc¹ | Jadivan L. de Oliveira MD¹ |
Marcelo Sá de Araújo MD¹ | Raphael L. C. de Araujo MD, PhD¹  |
Gustavo A. Laporte MD, PhD¹ | Claudio de Almeida Quadros MD, PhD¹ |
Alexandre F. de Oliveira MD, PhD¹ | Ademar Lopes MD, PhD¹

Qual o melhor “algoritmo de decisão”?

EQUIPE MULTIDISCIPLINAR

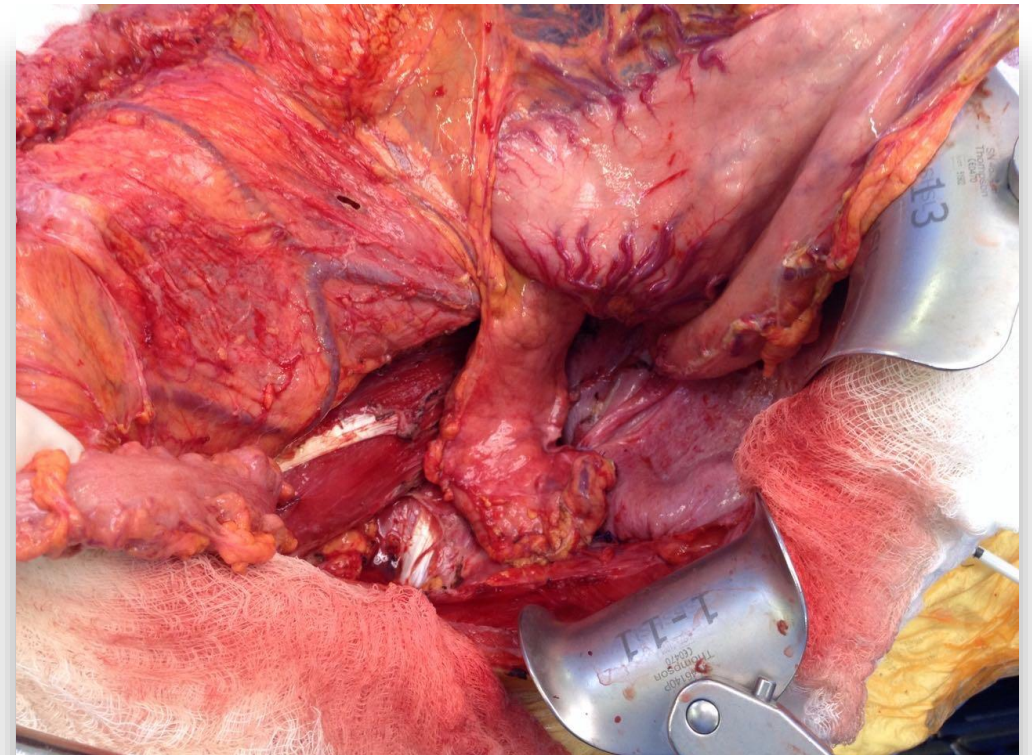


Centros de grande volume - ↑ Outcomes

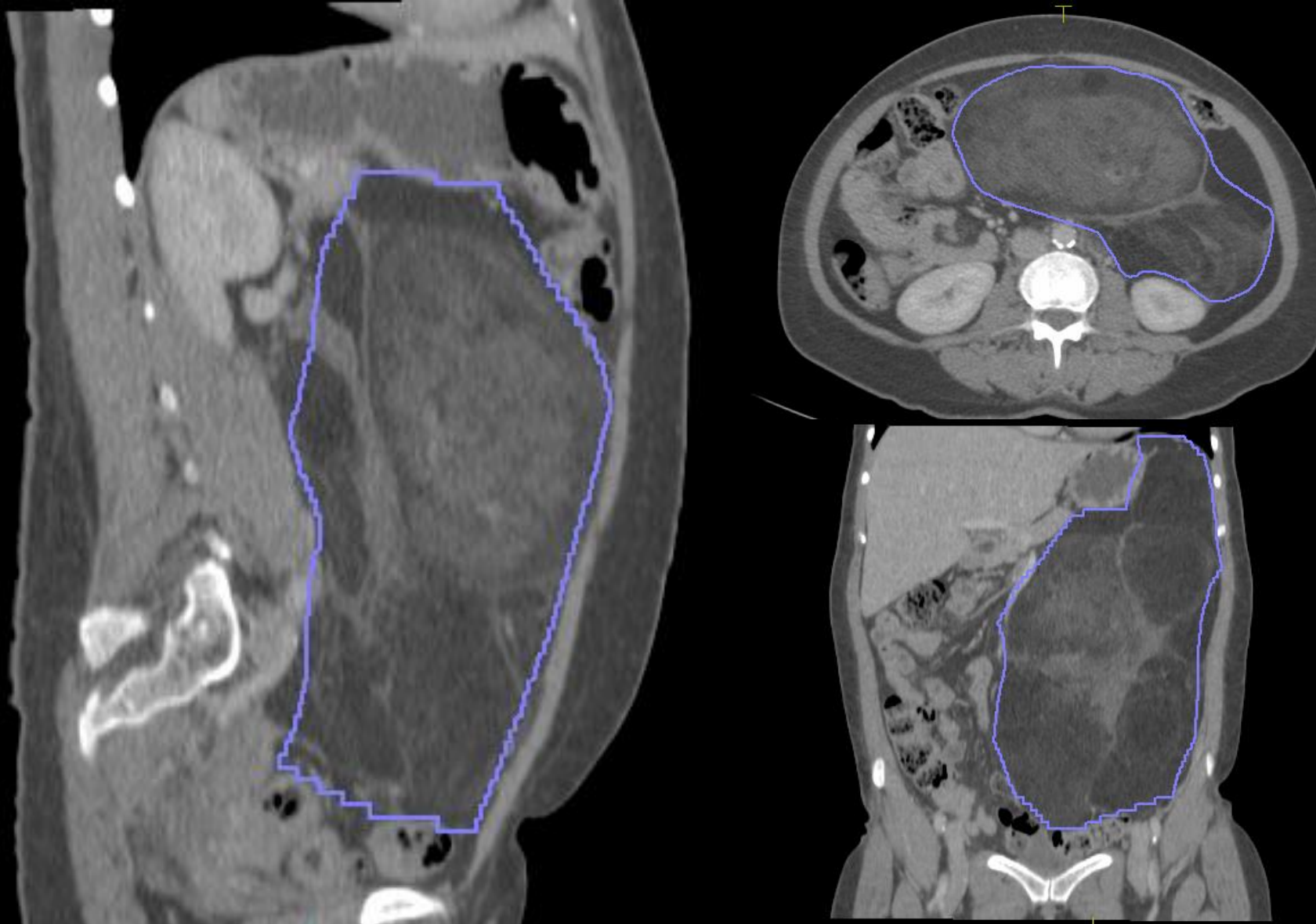


Retroperitônio

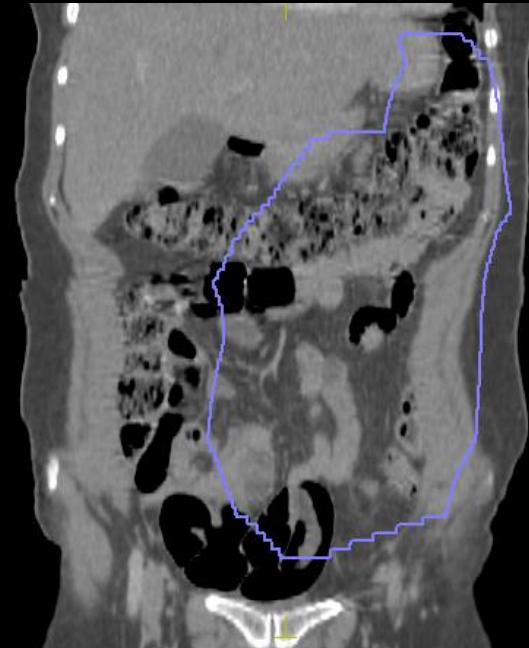
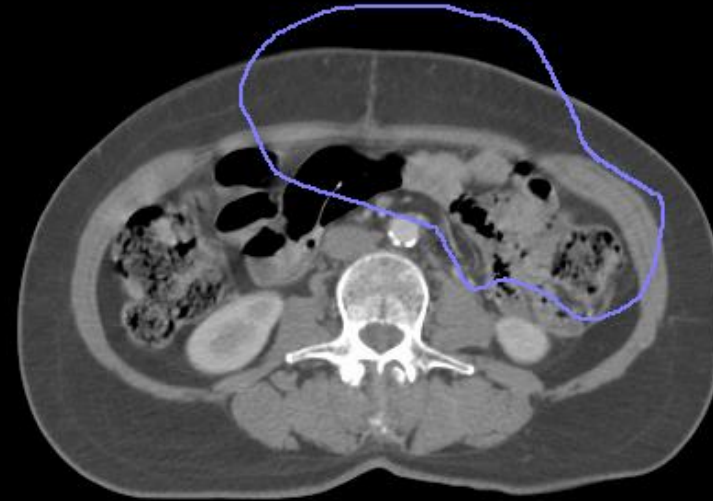
- Controle de margem macroscópica – ressecabilidade
- Controle de doença subclínica adjacente
- RP: Margens coincidentes
- População celular
- Preservação de órgãos



Racional da neoadjuvância

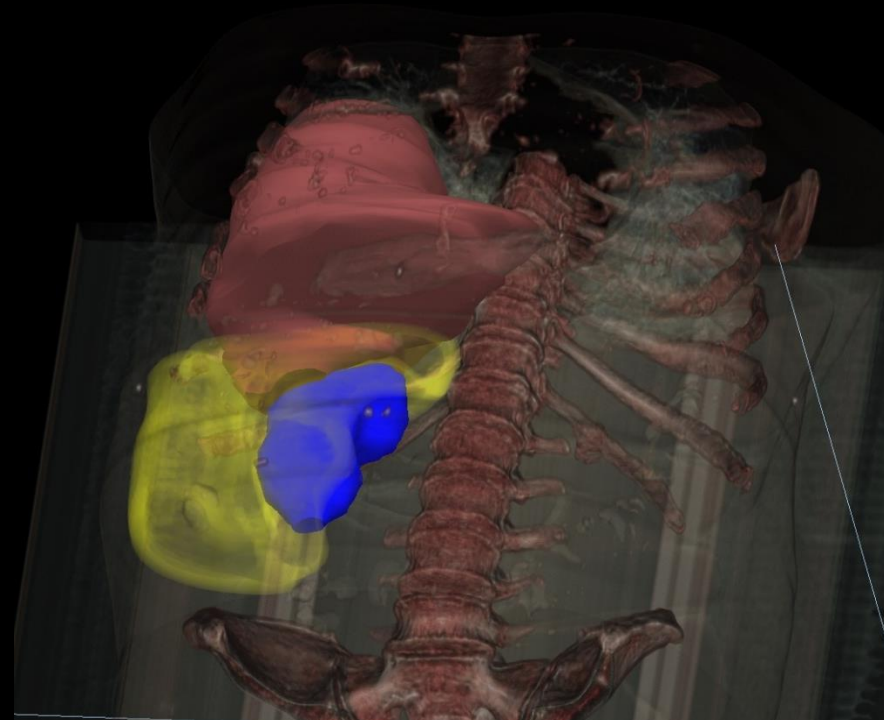
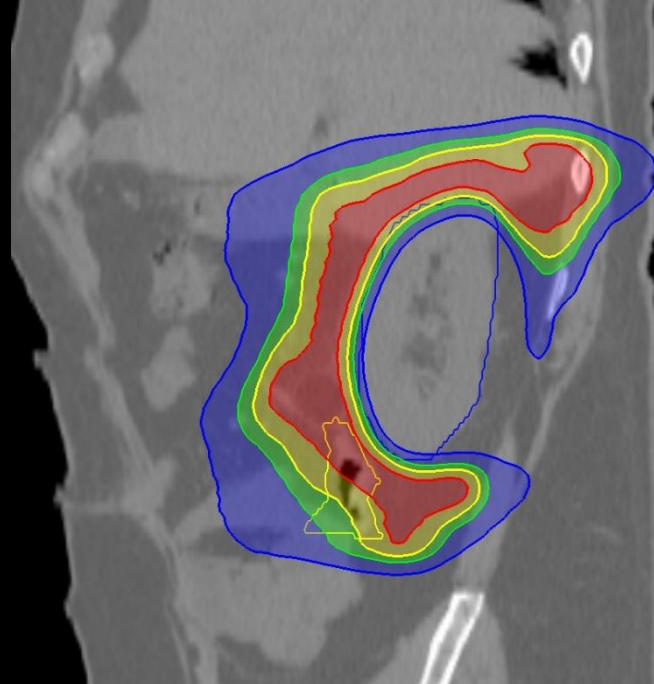
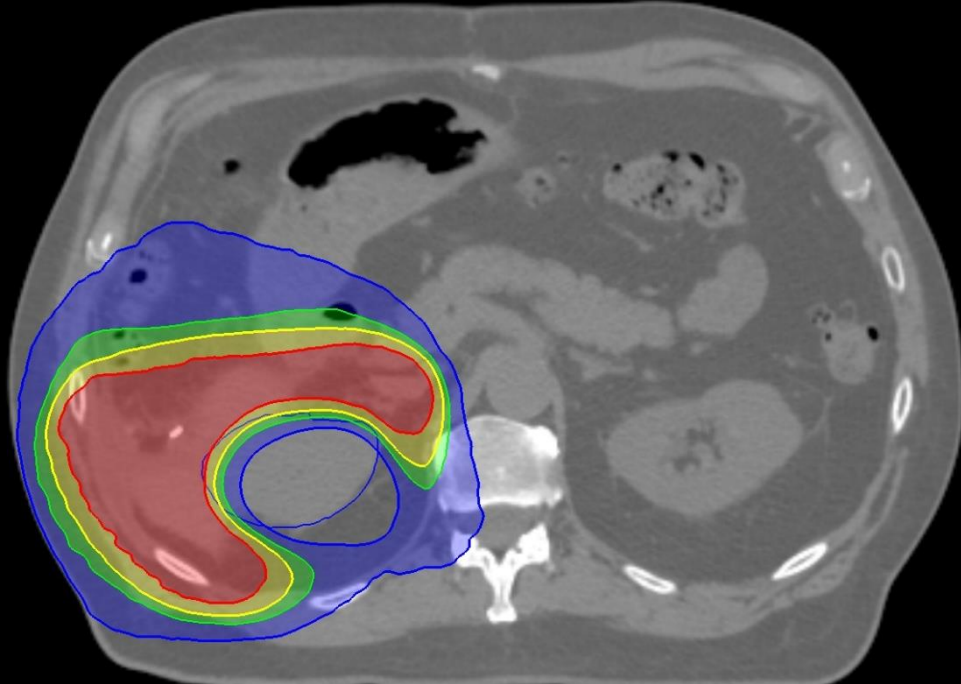


Desafio técnico

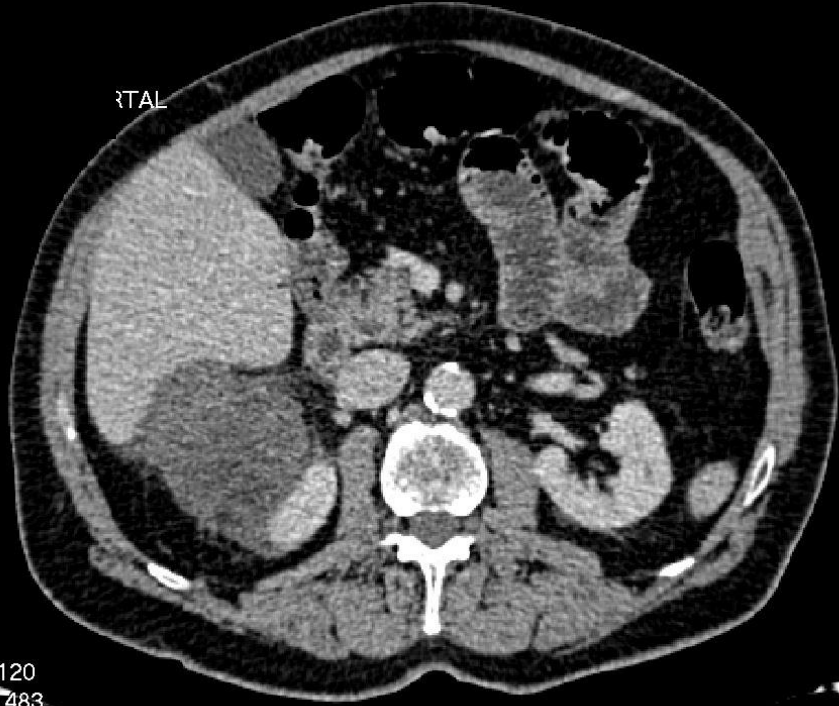
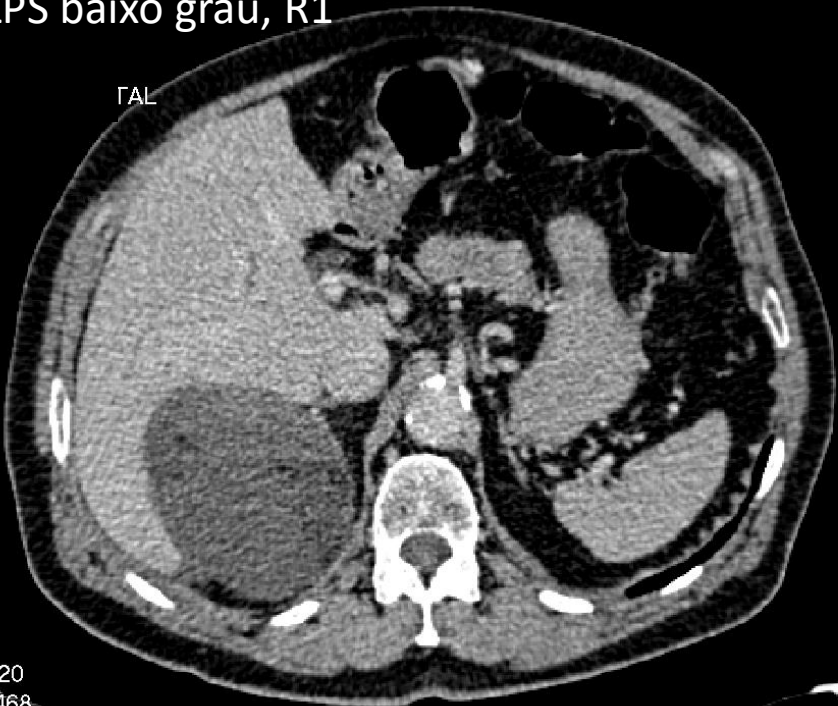


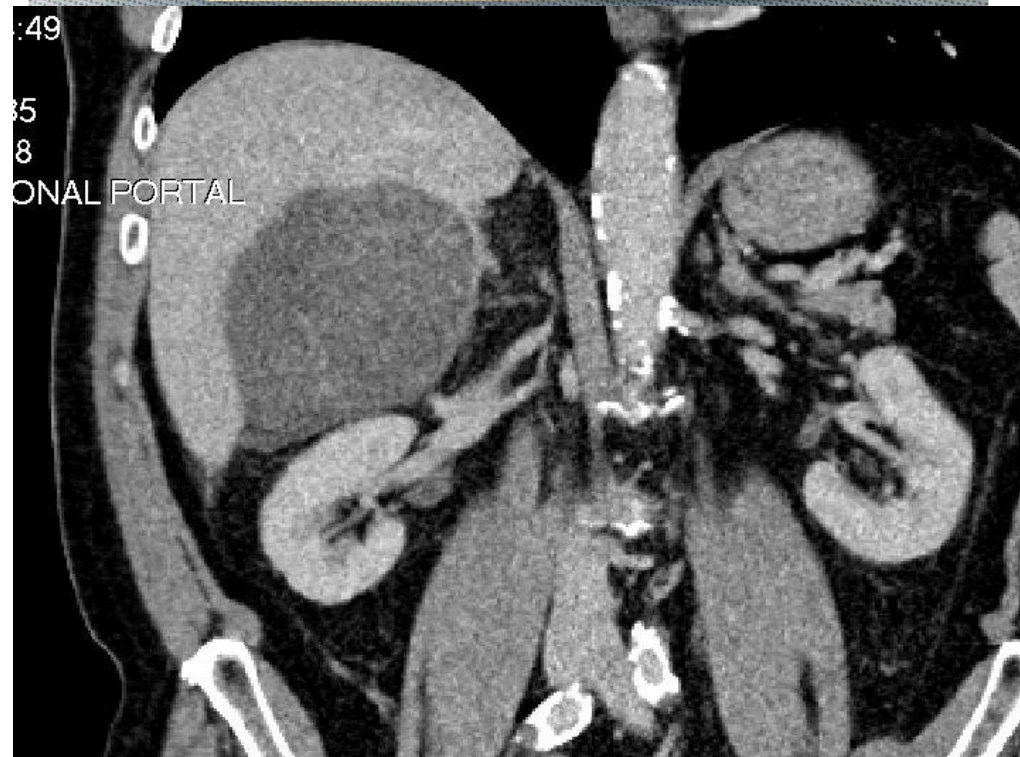
2019 - 63a, Lipo + desdiferenciação para S. pleomórfico e angiossarcoma, R0, QT

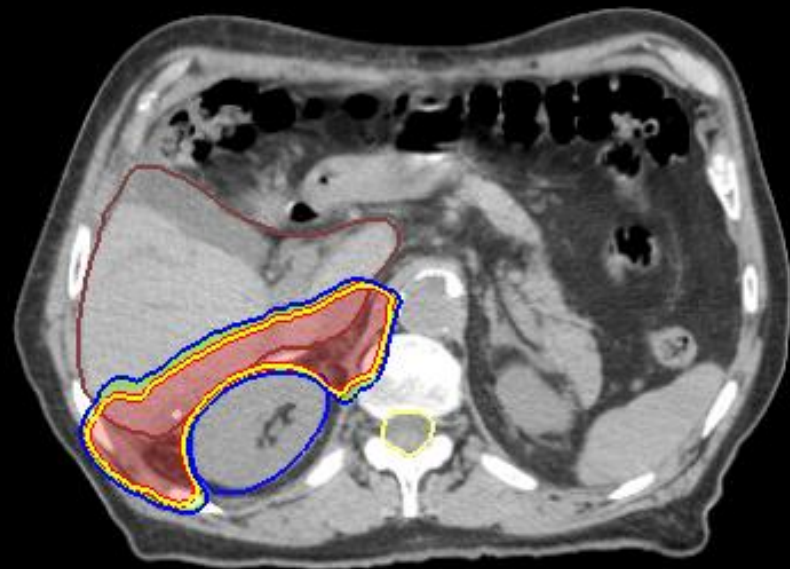
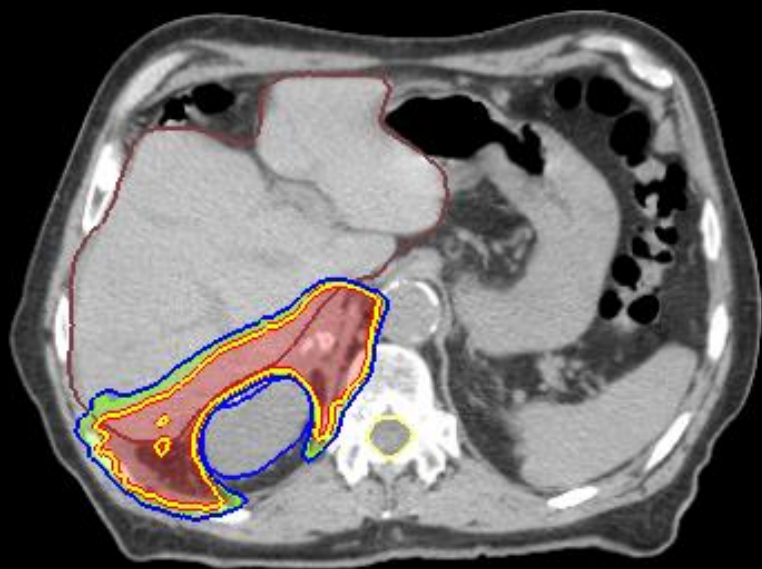




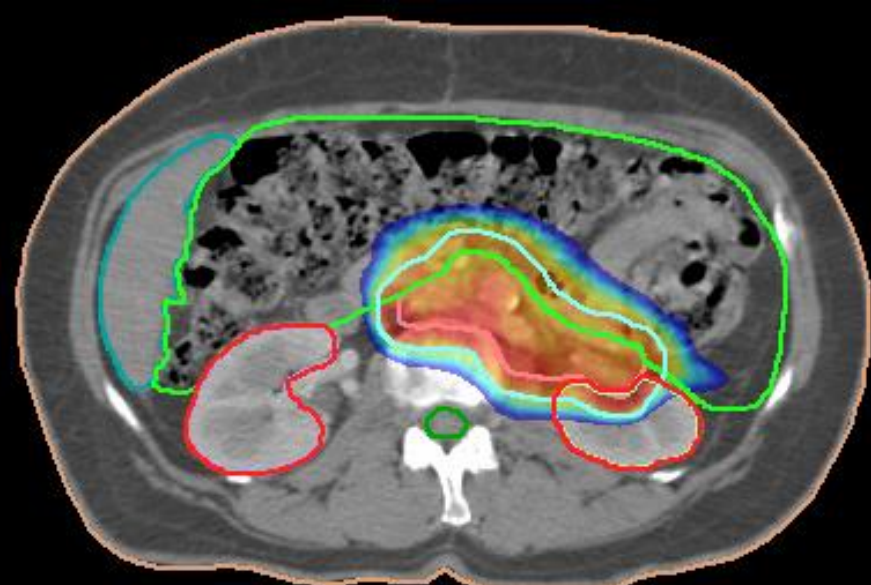
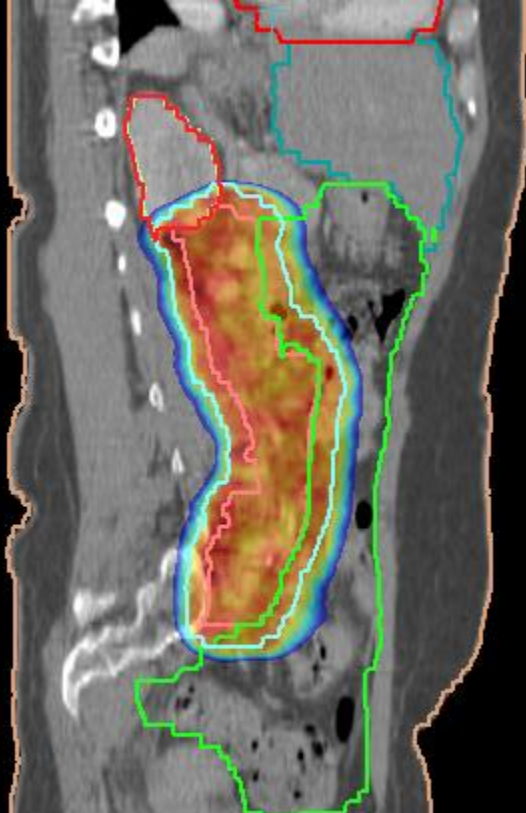
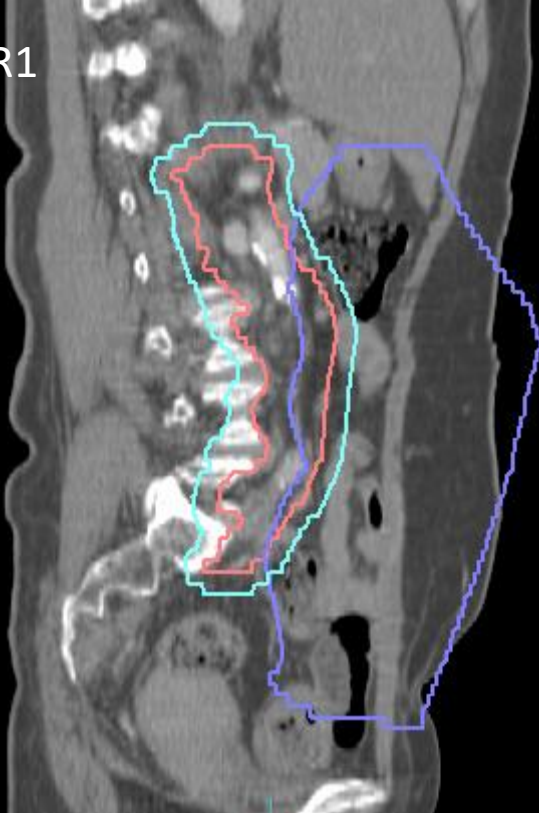
2019 - 75a, LPS baixo grau, R1





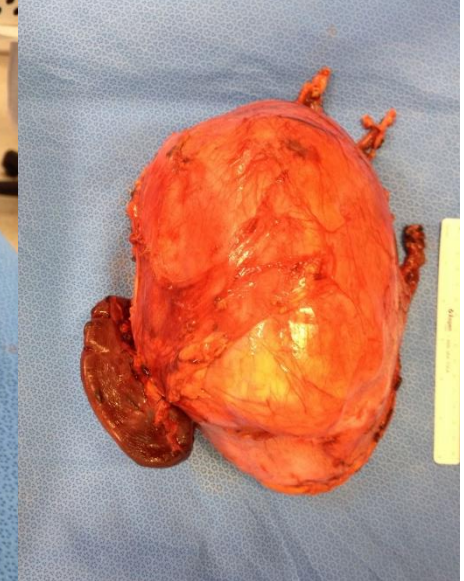
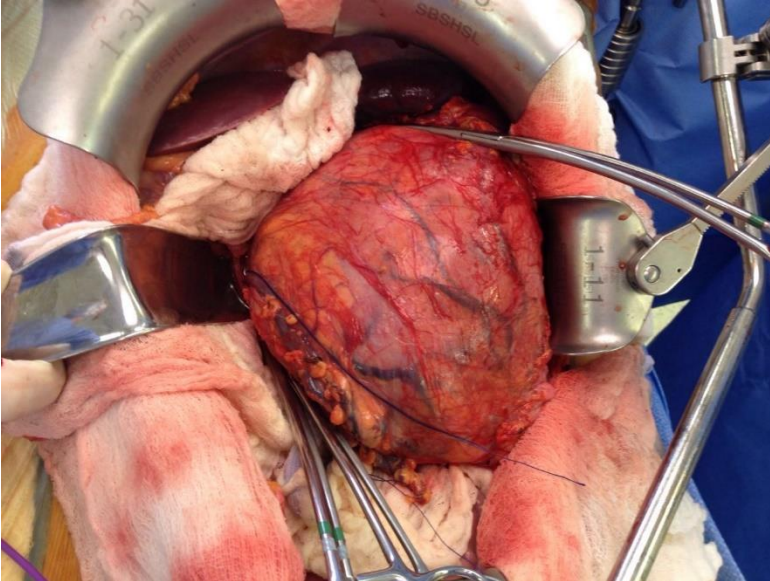
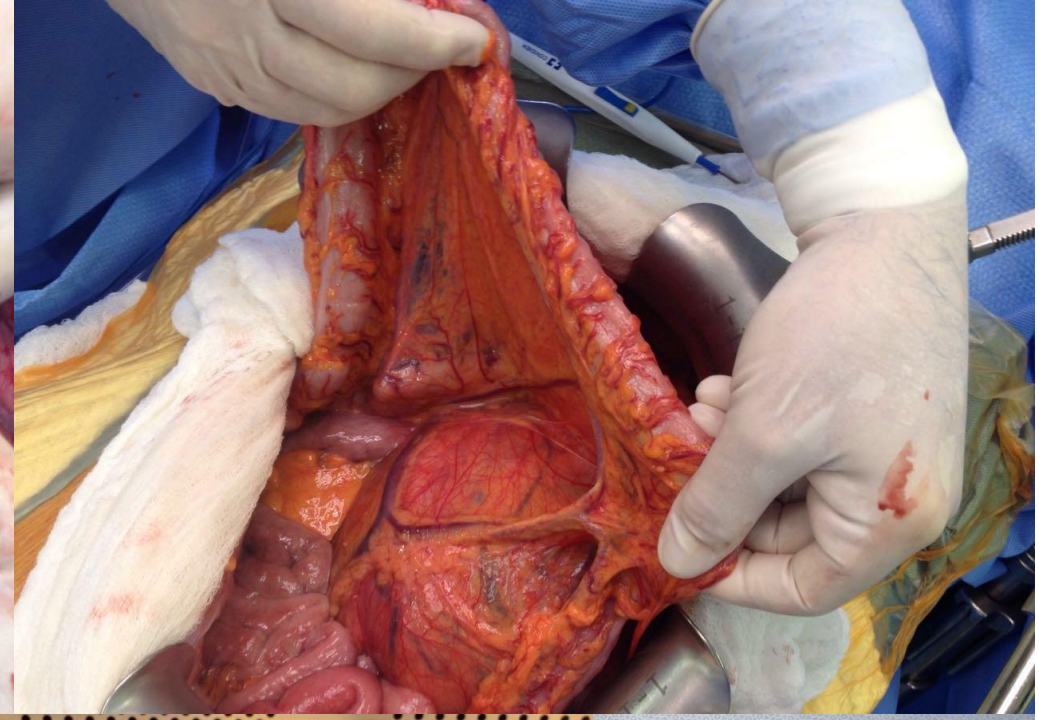
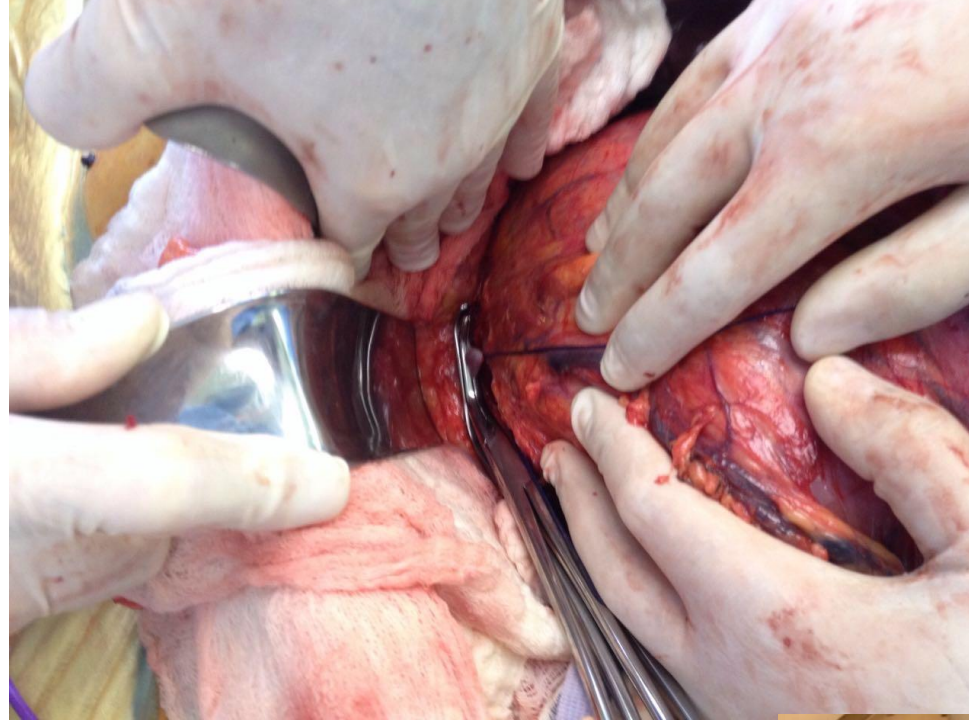


2017 - 42, LPS baixo grau, R1

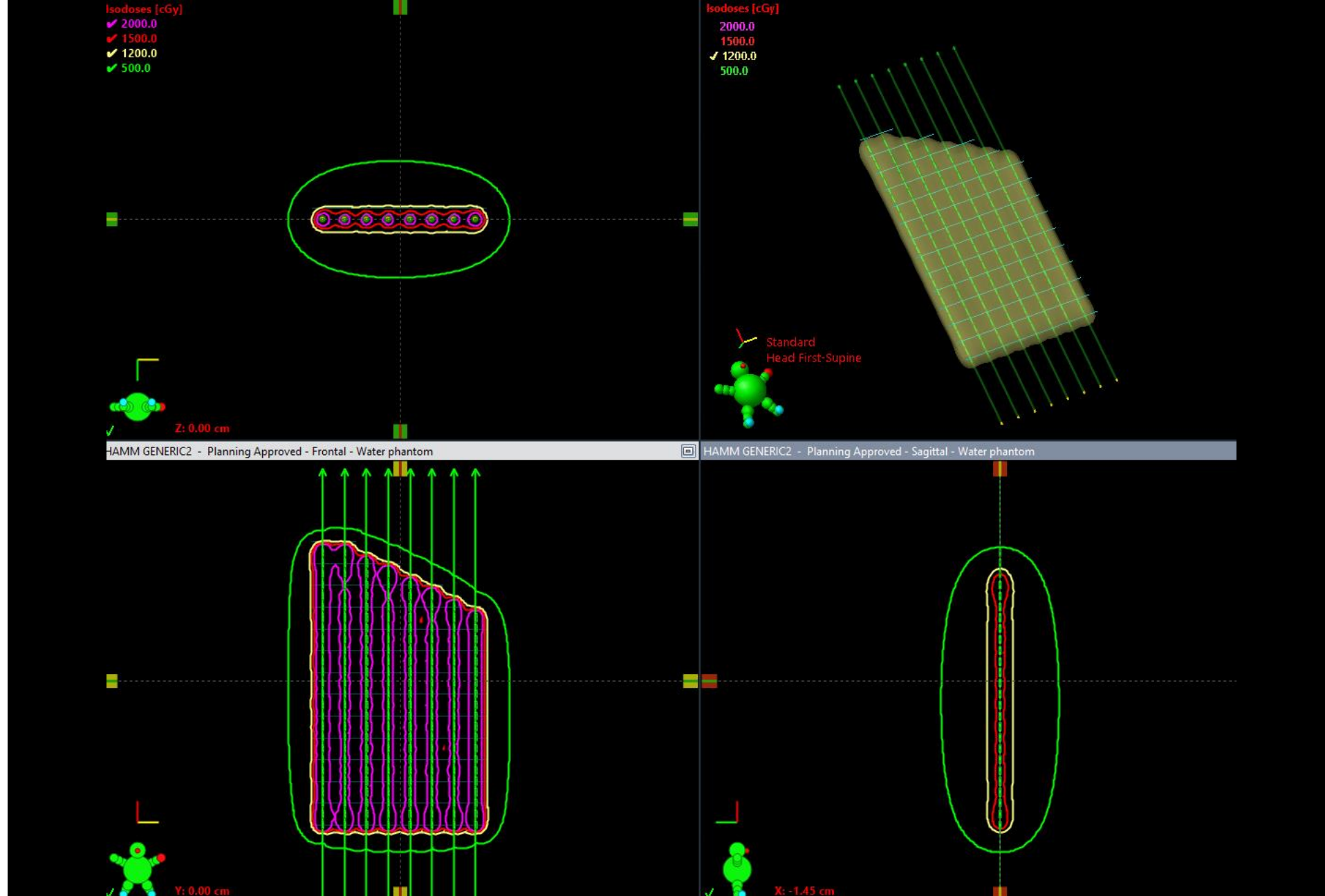


2016 - 61a, LPS desdiferenciado



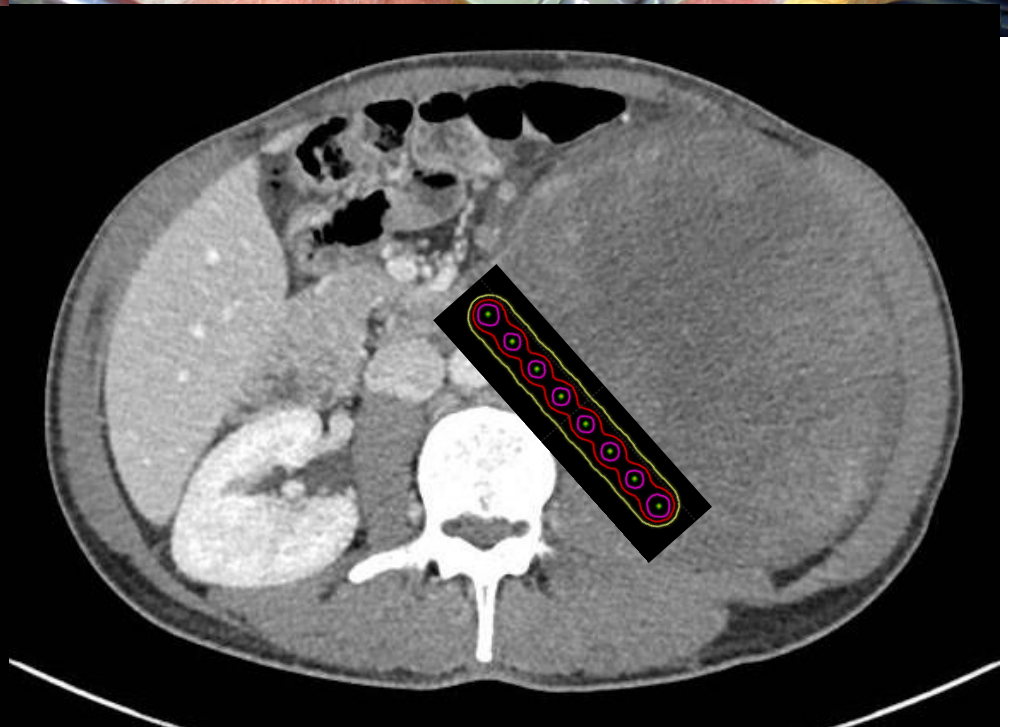
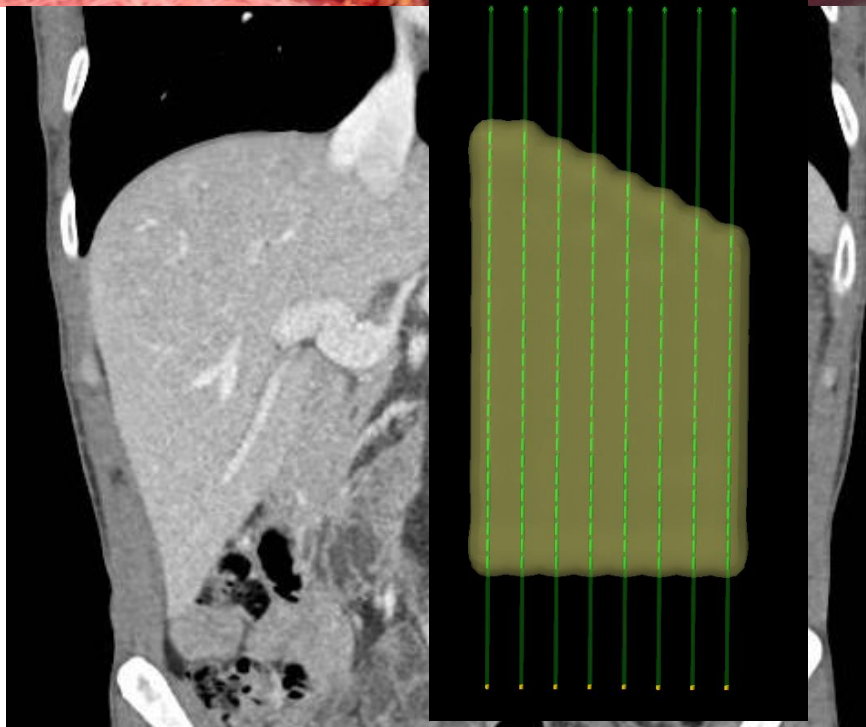
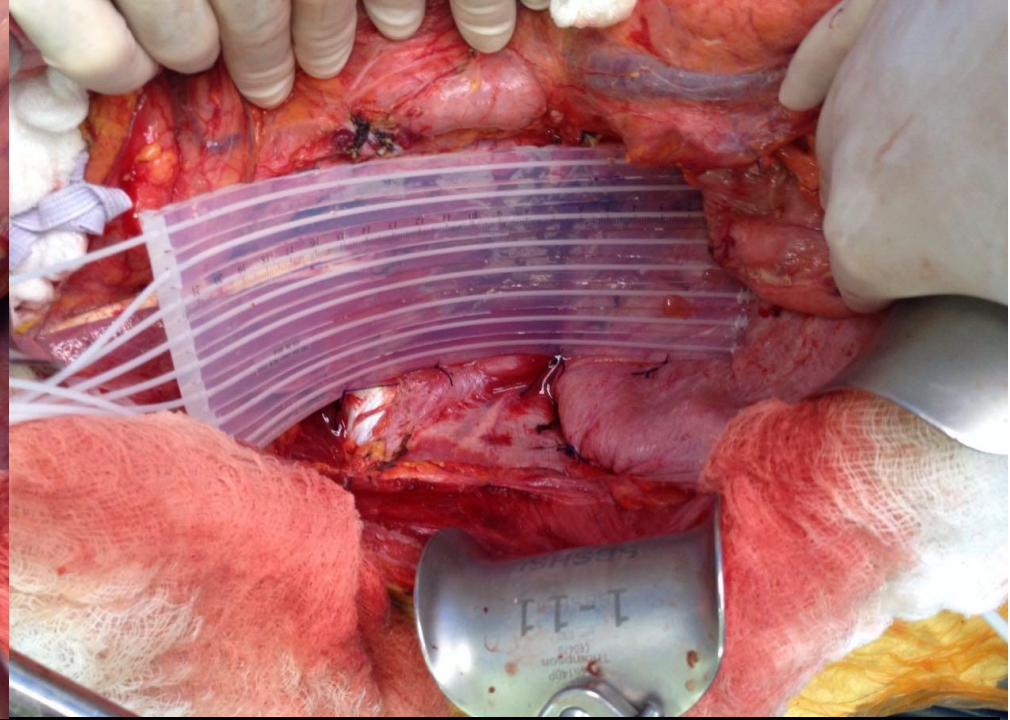
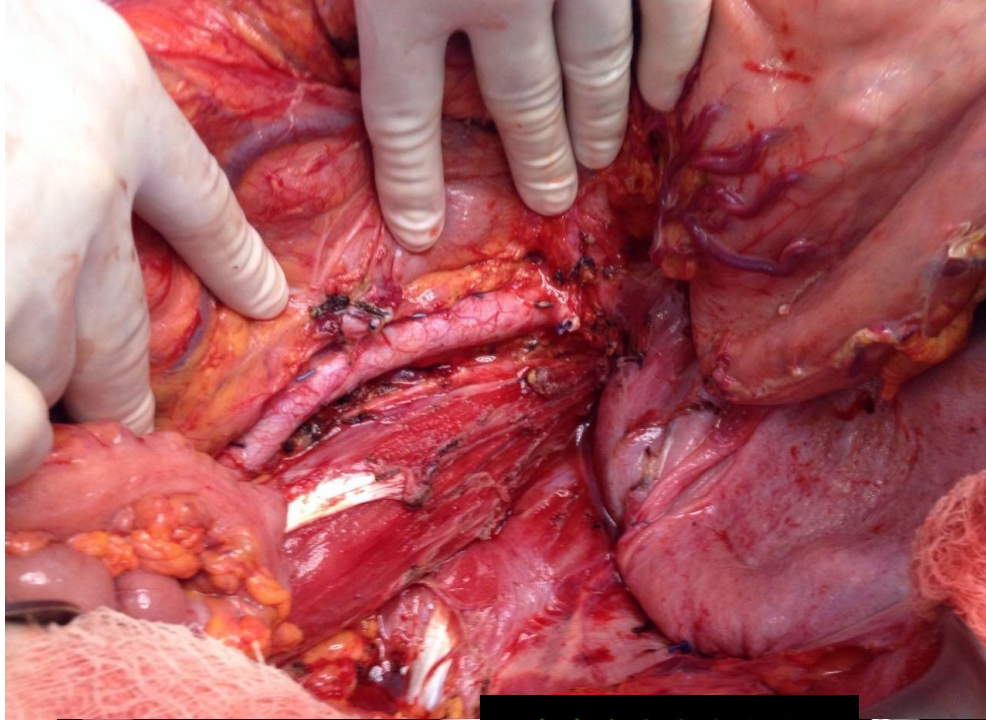


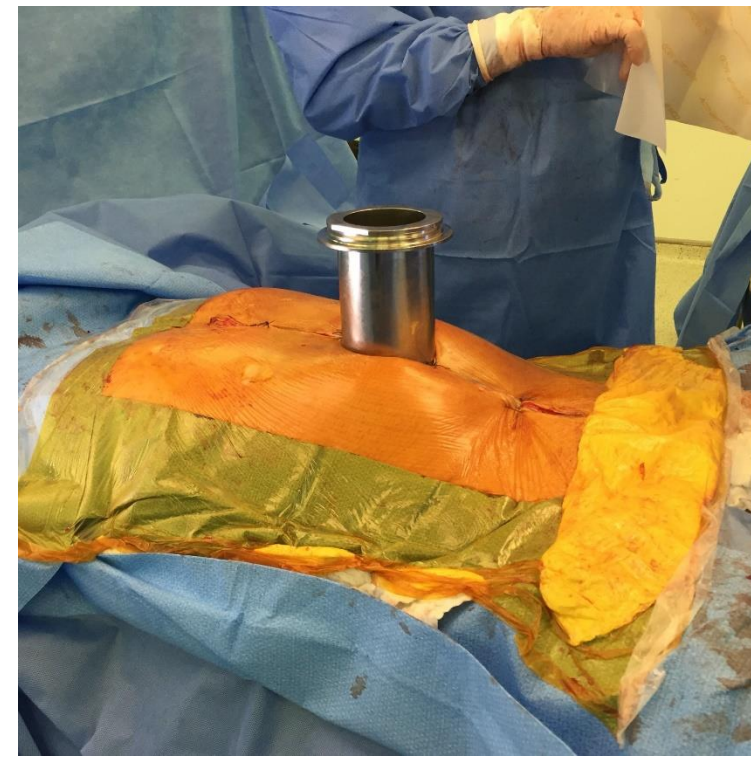
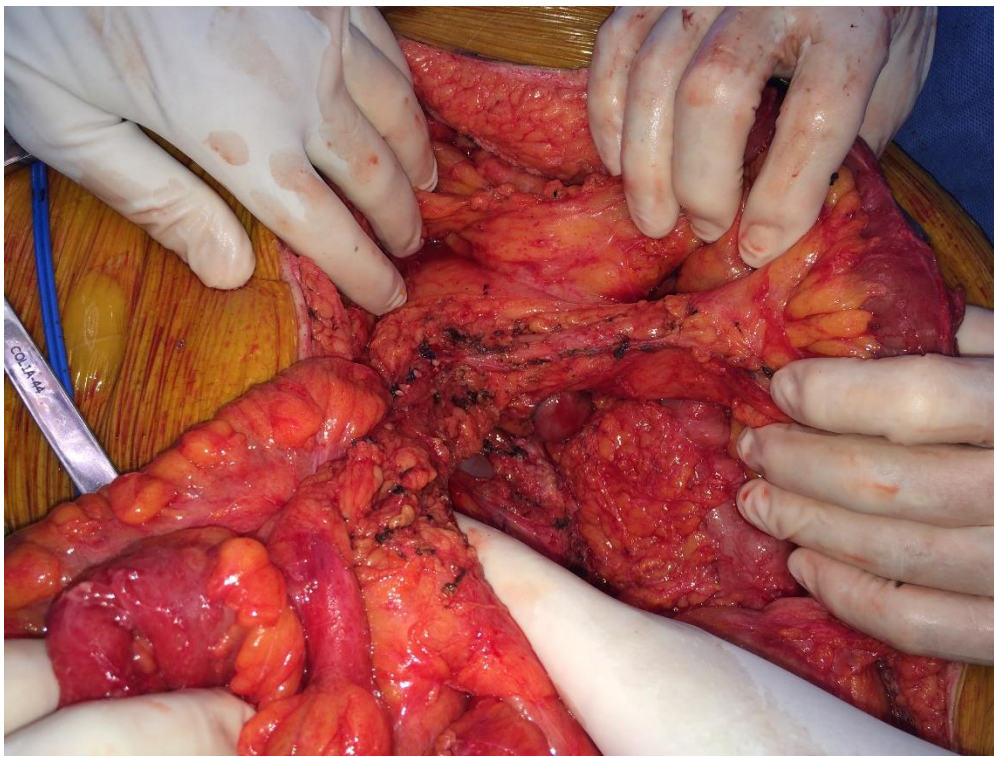
Hospital Sírio Libanês
Equipe: Dr. Fábio Ferreira, Dr. Benedito Rossi, Dr. Elton Leite. Créditos: Dr. João Luis F. da Silva



Hospital Sírio Libanês

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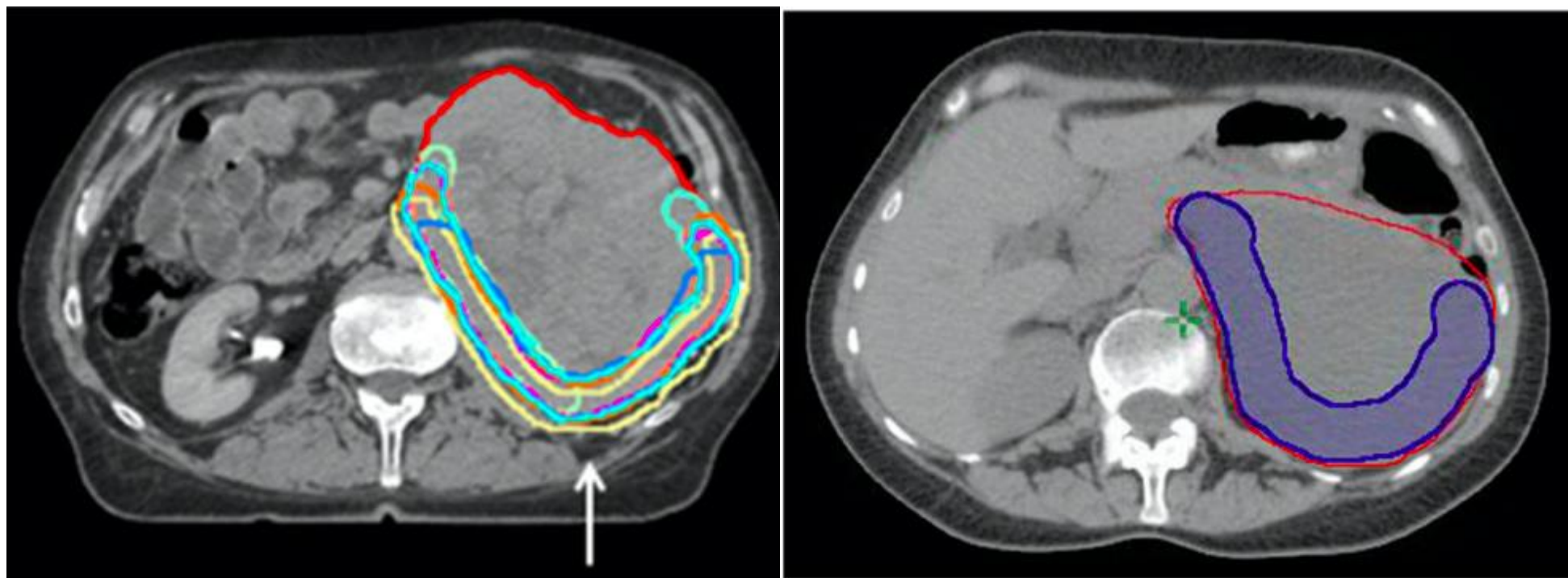
Elétrons:

- Tumores menores
- Recidivas
- Localização

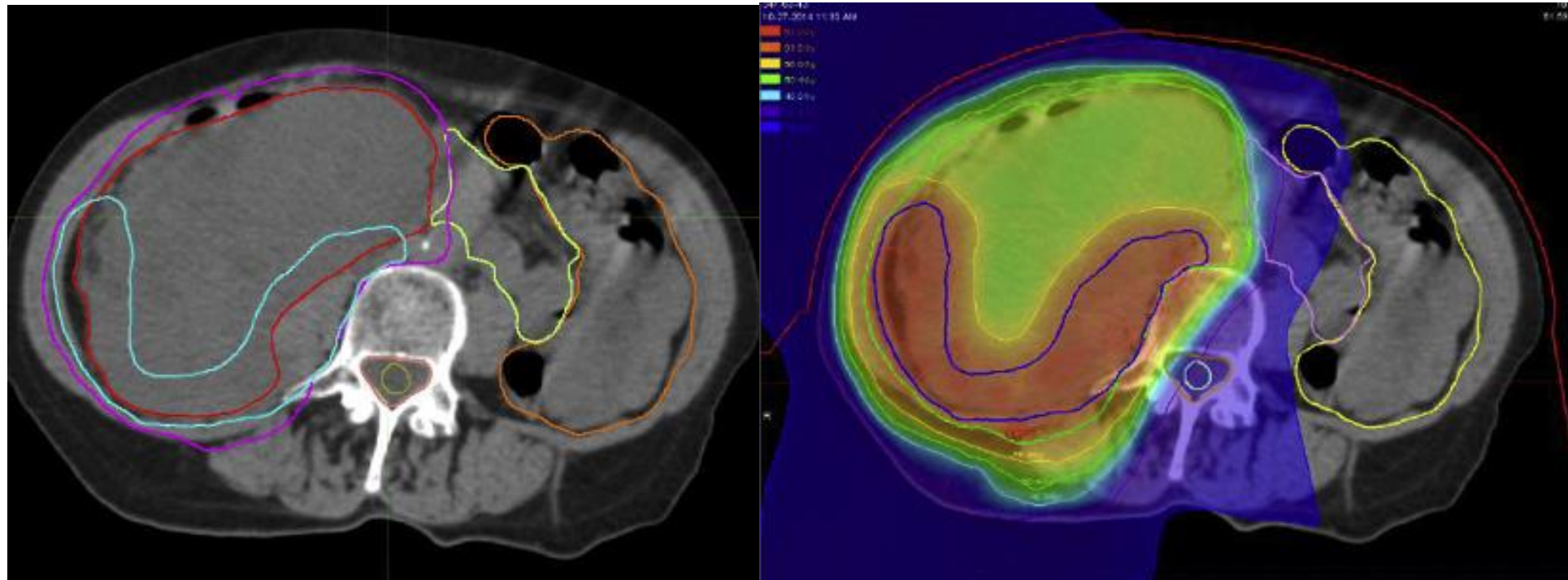


Definição de regiões de risco

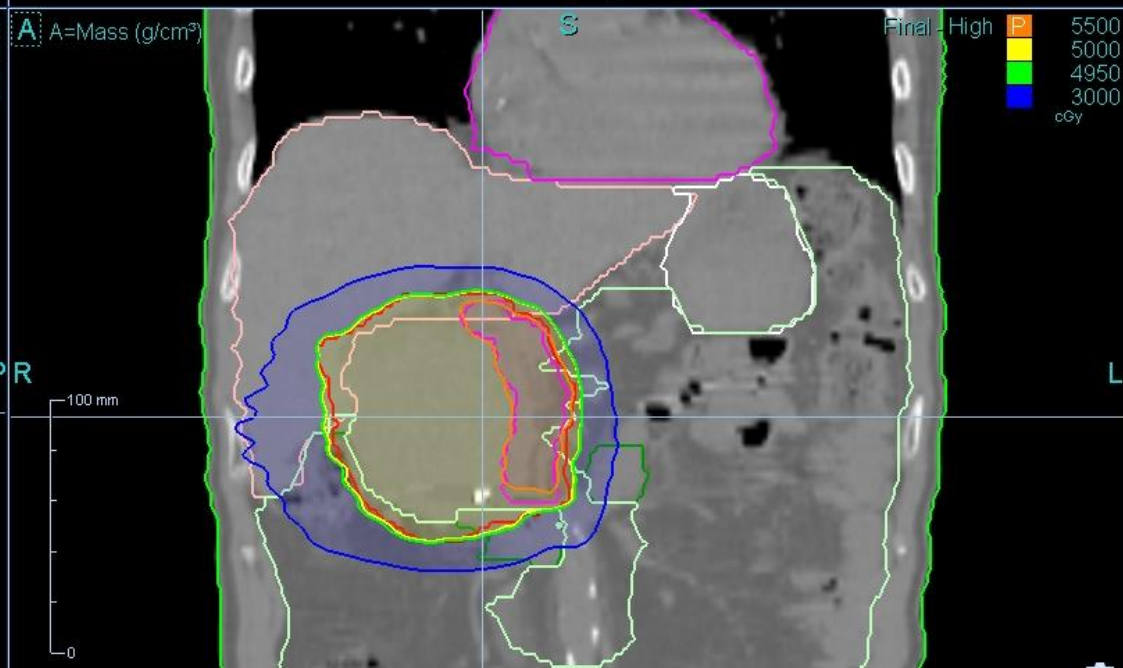
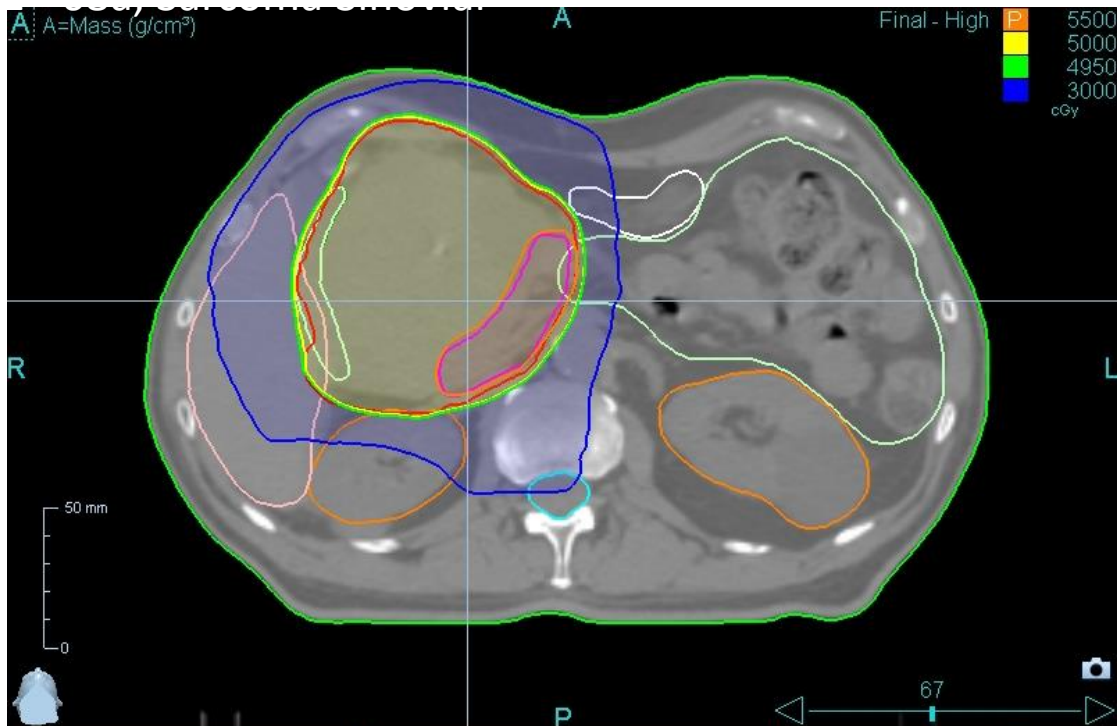
Concordância: Radio-oncologistas e cirurgiões oncológicos



Phase 1 trial - MGH



Acute radiation-related toxicities in study patients										
Grade	Nausea	Vomiting	Anorexia	Reflux	Diarrhea	Constipation	Flatulence	Fatigue	Skin	Neutropenia
0	3	6	7	10	9	9	10	2	2	10
1	5	4	2	1	2	2	1	6	9	1
2	3	1	2	0	0	0	0	3	0	0
3	0	0	0	0	0	0	0	0	0	0



Mensagens finais

- Cirurgia – principal tratamento
- Identificar pacientes que se beneficiam de RT
- RT pré-operatória vs RT pós operatória
- Decisão multidisciplinar
- Papel do IMRT e IGRT
- Hipofracionamento
- Intensificação do tratamento: escalonamento – SBRT em extremidades





Obrigado!

Elton Leite

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