VOLUMI CLINICI NEL TRATTAMENTO RADIOTERAPICO PRE-OPERATORIO DEI SARCOMI DELLE PARTI MOLLI DEGLI ARTI: ESPERIENZA DEL POLICLINICO S.ORSOLA-MALPIGHI

Dott.ssa A. Cortesi

S. Cammelli, A. Galuppi, S. Campagnoni, A. Arcelli,F. Labropoulos, A. Guido,
I. Ammendolia, G. Compagnone, A. Ferraro, G. Bianchi, M. Zompatori

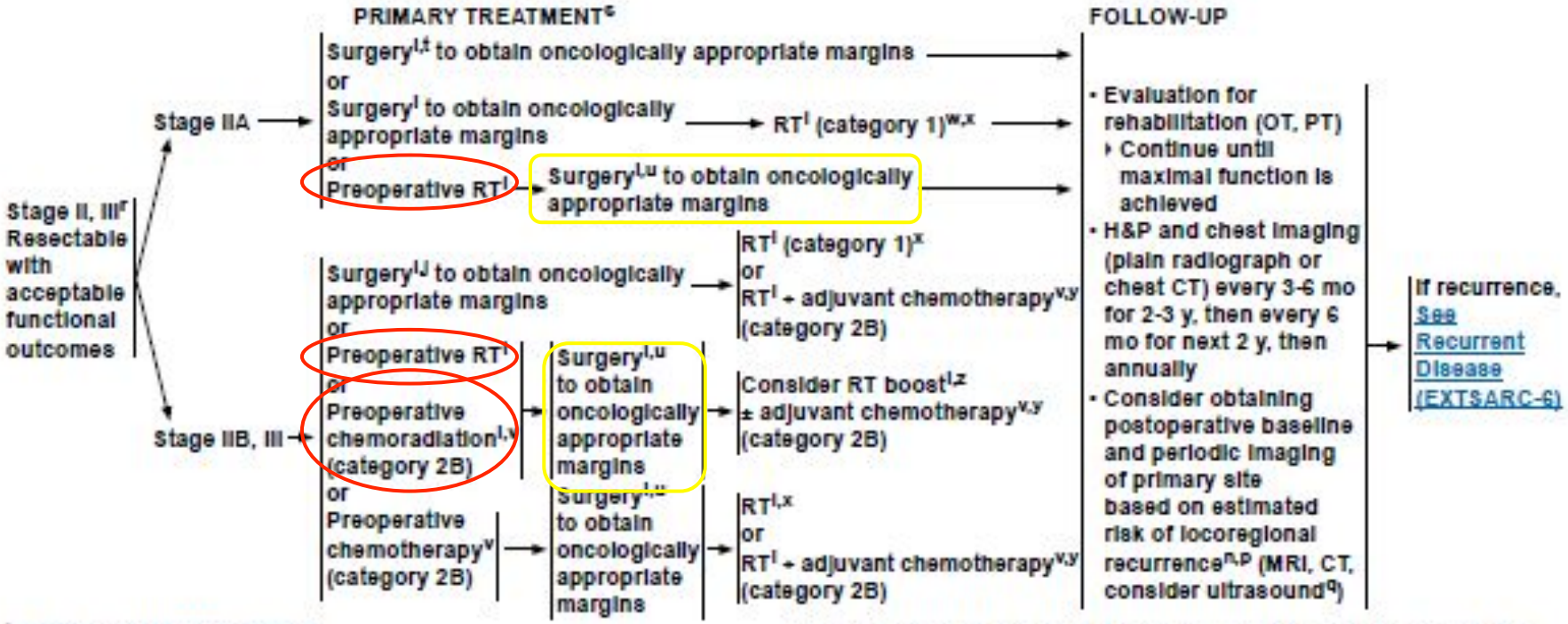
Rationale for preoperative radiotherapy

- Treatment volume is well-defined
- Improved quality of resection
- More conservative (function-sparing) surgery – downsizing
- Decreased risk of tumor seeding during resection
- Lower radiation dose (50 Gy vs 66-70 Gy)
- Reduction of late radiation morbidities (fibrosis, joint stiffness, edema)
- Better long term functional outcomes

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2014
Extremity/Superficial Trunk, Head/Neck

NCCN Guidelines Index
Soft Tissue Sarcoma, Table of Contents
Discussion



[l] See Principles of Surgery (SARC-C).

[j] In selected cases when margin status is uncertain, consultation with a radiation oncologist is recommended. Reresection, if feasible, may be necessary to render margins >1.0 cm.

[l] See Radiation Therapy Guidelines (SARC-D).

[n] In situations where the area is easily followed by physical examination, imaging may not be required.

[p] After 10 y, the likelihood of developing a recurrence is small and follow-up should be individualized.

[q] Consider ultrasound for smaller lesions that are superficial. Ultrasound should be done by an ultrasonographer experienced in musculoskeletal disease. (Choi H, Varma DGK, Fornage BD, Kim EE, et al. Soft-Tissue Sarcoma: MR Imaging vs Sonography for Detection of Local Recurrence After Surgery. AJR 1991;157:353-358.)

[r] Patients with stage III tumors with lymph node involvement should undergo regional lymph node dissection at the time of primary tumor resection ± RT.

[c] Treatment options for stage II and III should be made by a multidisciplinary team and involve consideration of the following: performance status, comorbid factors (including age), site of disease, histologic subtype, and institutional experience.

[t] Surgery alone may be an option for small tumors resected with wide margins.

[u] Consider re-imaging to assess primary tumor and to rule out metastatic disease.

[v] See Systemic Therapy Agents and Regimens with Activity in Soft Tissue Sarcoma (SARC-E).

[w] RT may be used in select circumstances such as close or positive margins where re-excision is not feasible or for functional considerations.

[x] Yang JC, Chang AE, Baker AR, et al. Randomized prospective study of the benefit of adjuvant radiation therapy in the treatment of soft tissue sarcomas of the extremity. J Clin Oncol 1998;16:197-203.

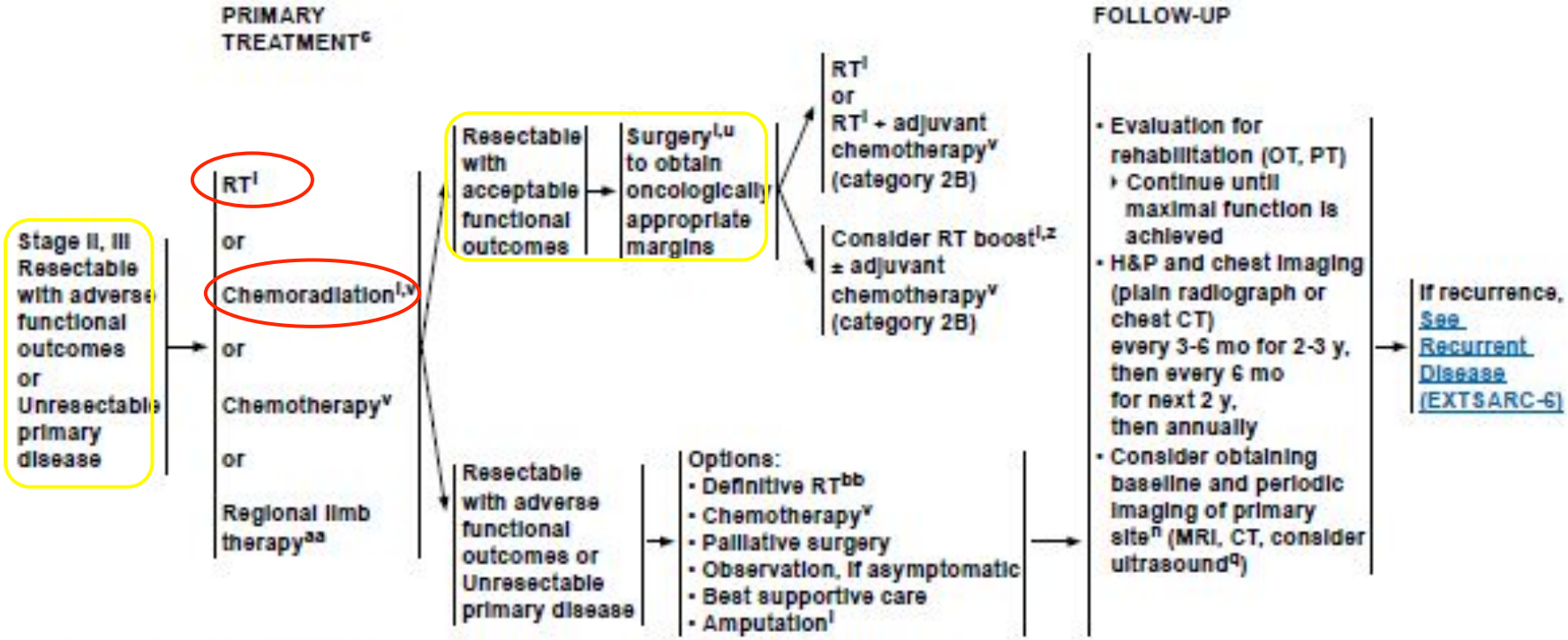
[y] There are limited and conflicting data regarding the potential benefits of adjuvant chemotherapy in stage II or stage III patients.

[z] For residual gross disease or microscopically positive margins.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

NCCN Guidelines Version 2.2014
Extremity/Superficial Trunk, Head/Neck

NCCN Guidelines Index
Soft Tissue Sarcoma Table of Contents
Discussion



[I] See Principles of Surgery (SARC-C).
[I] See Radiation Therapy Guidelines (SARC-D).
[N] In situations where the area is easily followed by physical examination, imaging may not be required.
[Q] Consider ultrasound for smaller lesions that are superficial. Ultrasound should be done by an ultrasonographer experienced in musculoskeletal disease. (Choi H, Varma DGK, Fornage BD, Kim EE, et al. Soft-Tissue Sarcoma: MR Imaging vs Sonography for Detection of Local Recurrence After Surgery. AJR 1991;157:353-358.)
[S] Treatment options for stage II and III should be made by a multidisciplinary team and involve consideration of the following: performance status, comorbid factors (including age), site of disease, histologic subtype, and institutional experience.
[U] Consider re-imaging to assess primary tumor and to rule out metastatic disease.
[V] See Systemic Therapy Agents and Regimens with Activity in Soft Tissue Sarcoma (SARC-E).
[Z] For residual gross disease or microscopically positive margins.
[AA] Should only be done at institutions with experience in regional limb therapy.
[BB] Definitive RT entails delivering the maximal local dose compatible with known normal tissue tolerance, typically in the range of 7000-8000 cGy with sophisticated treatment planning techniques being a necessity in this setting.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Table 1
Patient characteristics.

	High grade	Low grade
n	38	12
Gender		
Male	49%	75%
Female	51%	25%
Median Age (years)	62.5	39
Tumor site		
Lower Extremity	25 (66%)	10 (83%)
Upper Extremity	10 (26%)	–
Trunc	3 (8%)	2 (17%)
FNLCC grade		
Not applicable	1 (3%)	1 (8%)
Grade 1	–	11 (92%)
Grade 2	10 (26%)	–
Grade 3	27 (71%)	–
Histology		
Pleomorphic/Undifferentialted	10 (26%)	–
Leiomyosarcoma	8 (21%)	–
Myxoid liposarcoma	–	7 (58%)
Liposarcoma – other	4 (11%)	–
Fibromyxoid	–	3 (25%)
Myxofibrosarcoma	6 (16%)	–
MPNST	5 (13%)	–
Synovial	4 (11%)	–
Other	1 (3%)	2 (17%)

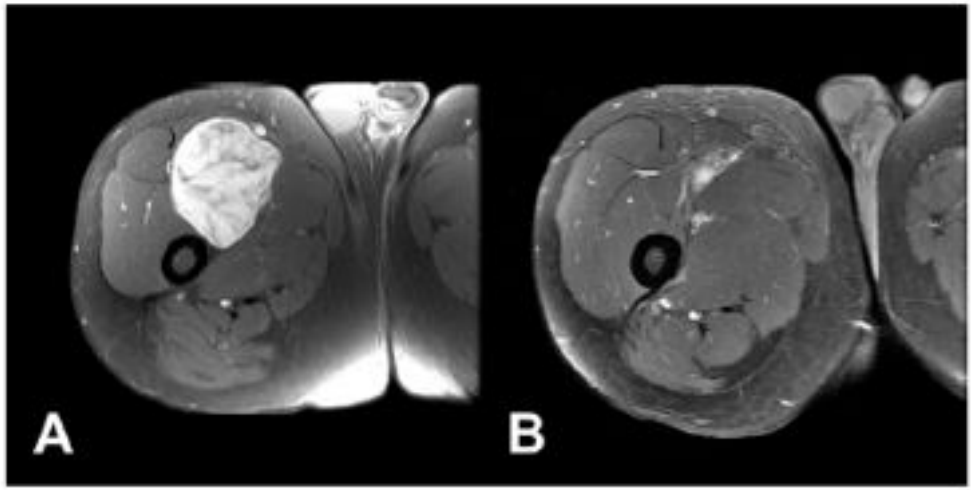


Fig. 2. Axial T1 Gadolinium of a myxoid liposarcoma before (A) and after (B) radiotherapy.

e following pre-operative radiotherapy

Table 2
Tumor volumes.

	High grade	Non-myxoid low grade	Myxoid liposarcoma
Mean pre-treatment volume (cm^3)	150.0	676.8	199.8
Mean post-treatment volume (cm^3)	180.8	588.7	77.1
Median absolute volume change (cm^3)	−0.1	−13.1	−114.0
Median relative volume change (%)	−0.5	−13.8	−82.1


Radiotherapy and Oncology

Radiological and pathological response following pre-operative radiotherapy for soft-tissue sarcoma

ELSEVIER

International Journal of Radiation Oncology*Biology*Physics

Volume 72, Issue 1, Supplement, 1 September 2008, Pages S506–S507

Proceedings of the American Society for Therapeutic Radiology and Oncology 50th Annual Meeting

American Society for Therapeutic Radiology and Oncology 50th Annual Meeting

Poster Viewing Presentation

Evaluation of Radiological and Pathological Response Following Pre-operative Radiotherapy of Soft-tissue Sarcoma

D. Roberge, T. Skamene, A. Nahal, R. Turcotte, C. Freeman

The median time from the initial MRI to the start of radiotherapy was 21.5 days. The median time from the end of the radiotherapy to the second MRI was 22 days. The median time from post-treatment MRI to the surgery was 7 days. **Changes in tumor volume varied from a decrease of 88% to an increase of 100%. The median decrease in tumor volume was 37% for low-grade sarcomas and 4% for high-grade sarcomas** (p = 1.0). A partial response on MRI (VR ≥50%) was highly predictive of a good pathological response (p < 0.001). Patients with stable disease on imaging had wide ranging pathological responses (0-95%). Imaging progression (volume increase ≥25%) did not predict poor pathological response (range 0-60%, p = 0.15).


International Journal of Radiation Oncology•Biology•Physics

Evaluation of Radiological and Pathological Response Following Pre-operative Radiotherapy of Soft-tissue Sarcoma

Integrative Oncology

Bedi et al., J Integr Oncol 2013, 2:2
http://dx.doi.org/10.4172/2329-6771.1000109

Review Article

Tumor Increase on MRI after Neoadjuvant Treatment is Associated with Greater Pathologic Necrosis and Poor Survival in Patients with Soft Tissue Sarcoma

Meena Bedi, Jordan Kharofa, Eduardo V Zambrano, Jason Chang, Keith Baynes, Alan P Mautz, Melissa DuBois, David M King, Donald A Hackbarth and Dian Wang*

Department of Radiation Oncology, Medical College of Wisconsin, 8701 Watertown Plank Rd, Milwaukee, WI 53045, USA

Complete Response	Disappearance of all target lesions
Partial Response	30% decrease in sum of longest dimension of target lesions
Stable Disease	Decrease in tumor size of <30% or an increase of <20%
Progressive Disease	Increase of ≥ 20% in the sum of the longest dimensions of target lesions

Table 1: RECIST criteria.

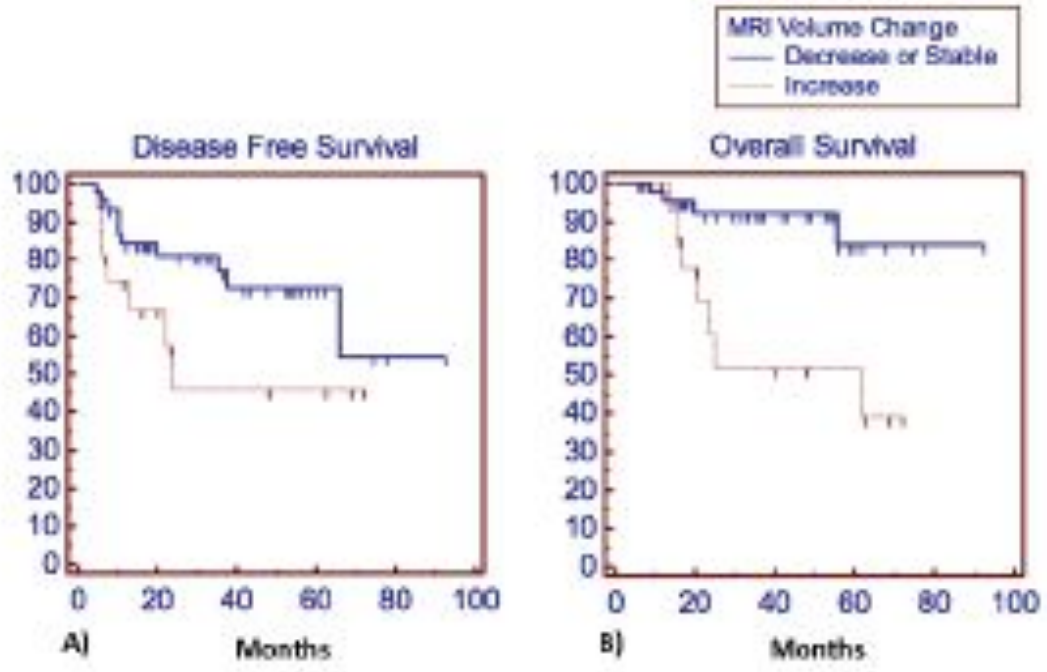


Figure 1: Relationship between MR-based volume change and survival [disease free survival (1A) and overall survival (1B)].

Tumor Increase on MRI after Neoadjuvant Treatment is Associated with Greater Pathologic Necrosis and Poor Survival in Patients with Soft Tissue Sarcoma

Median tumor volume decreased of 15,08 cm^3

Conclusions

MR-based increase in tumor volume and size after neoadjuvant radiotherapy is associated with greater percent necrosis and less fibrosis on pathology. Patients with a high percentage of necrosis following neoadjuvant radiotherapy with or without sequential neoadjuvant chemotherapy are more likely to have high grade tumors and worse survival. Further evaluation of post-radiotherapy fibrosis might be useful to predict survival outcomes.

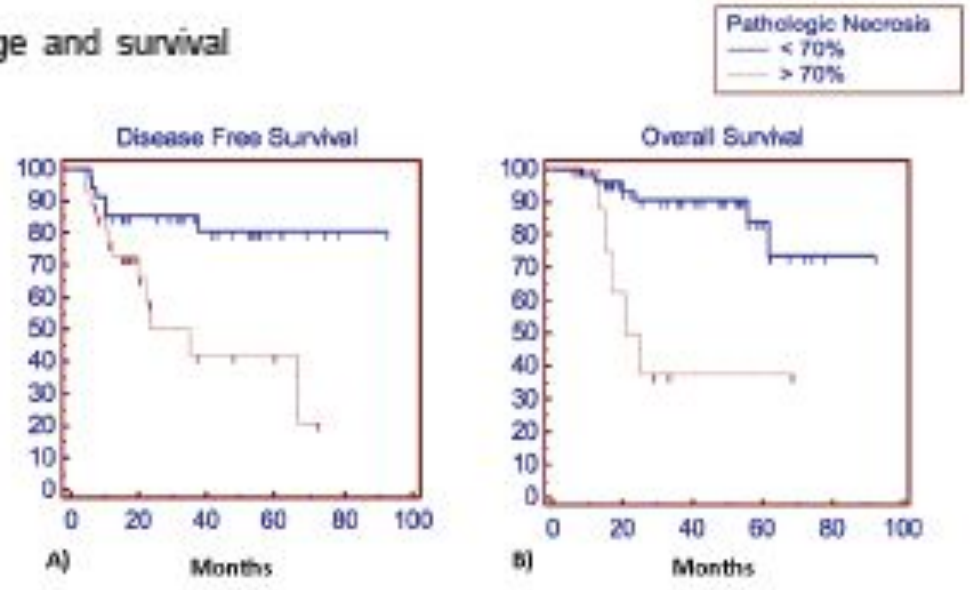


Figure 2: Relationship between percent pathologic necrosis and survival [disease free survival (2a) and overall survival (2b)].

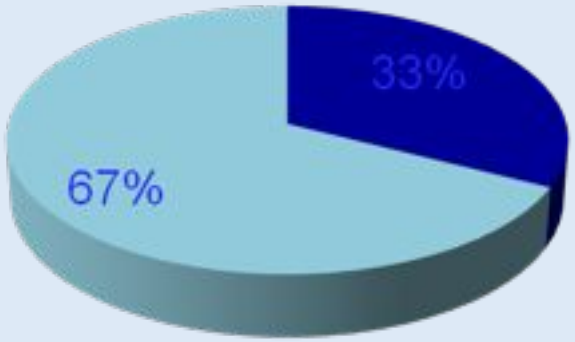
Our experience

Materials and methods

From January 2005 to January 2014

83 patients

Median age: 59 years (23-87)



NEOADJUVANT RTE + CT

CT: Epirubicina + Ifosfamide/Doxorubicina

50 Gy / 25 fx

+ boost 20 Gy if R1 (marginal or intralesional)

CTV =

GTV +

4 cm cranial-caudal

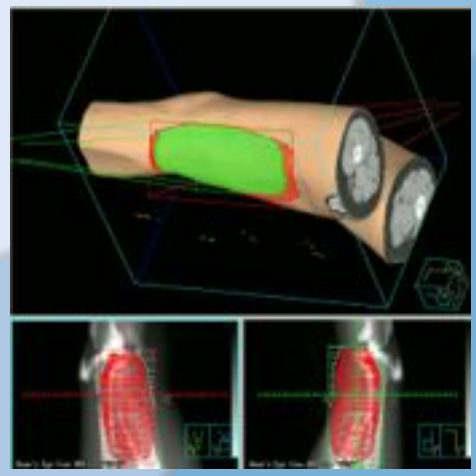
- 1 cm AP
- 1 cm LL

PTV=

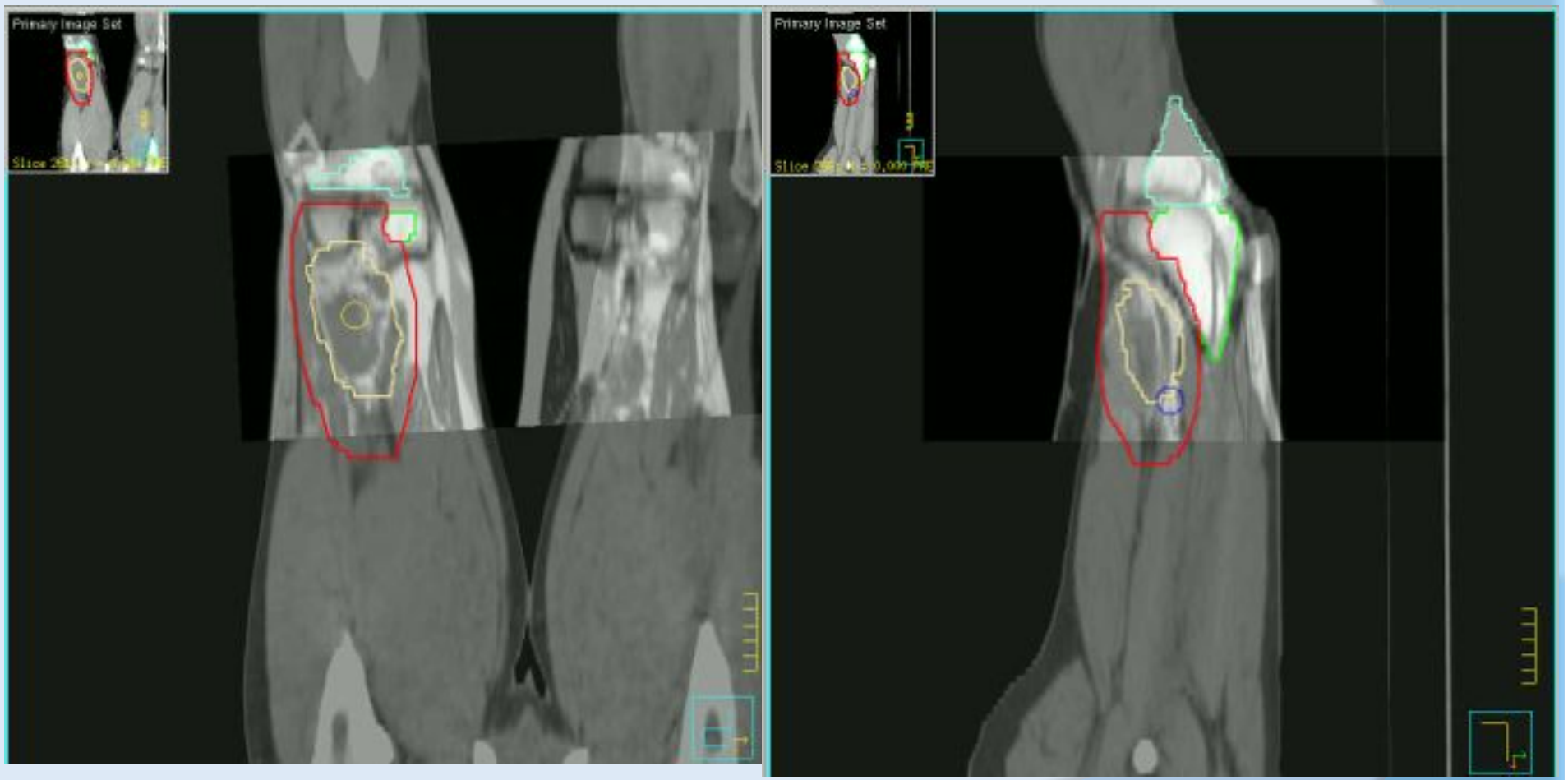
CTV +

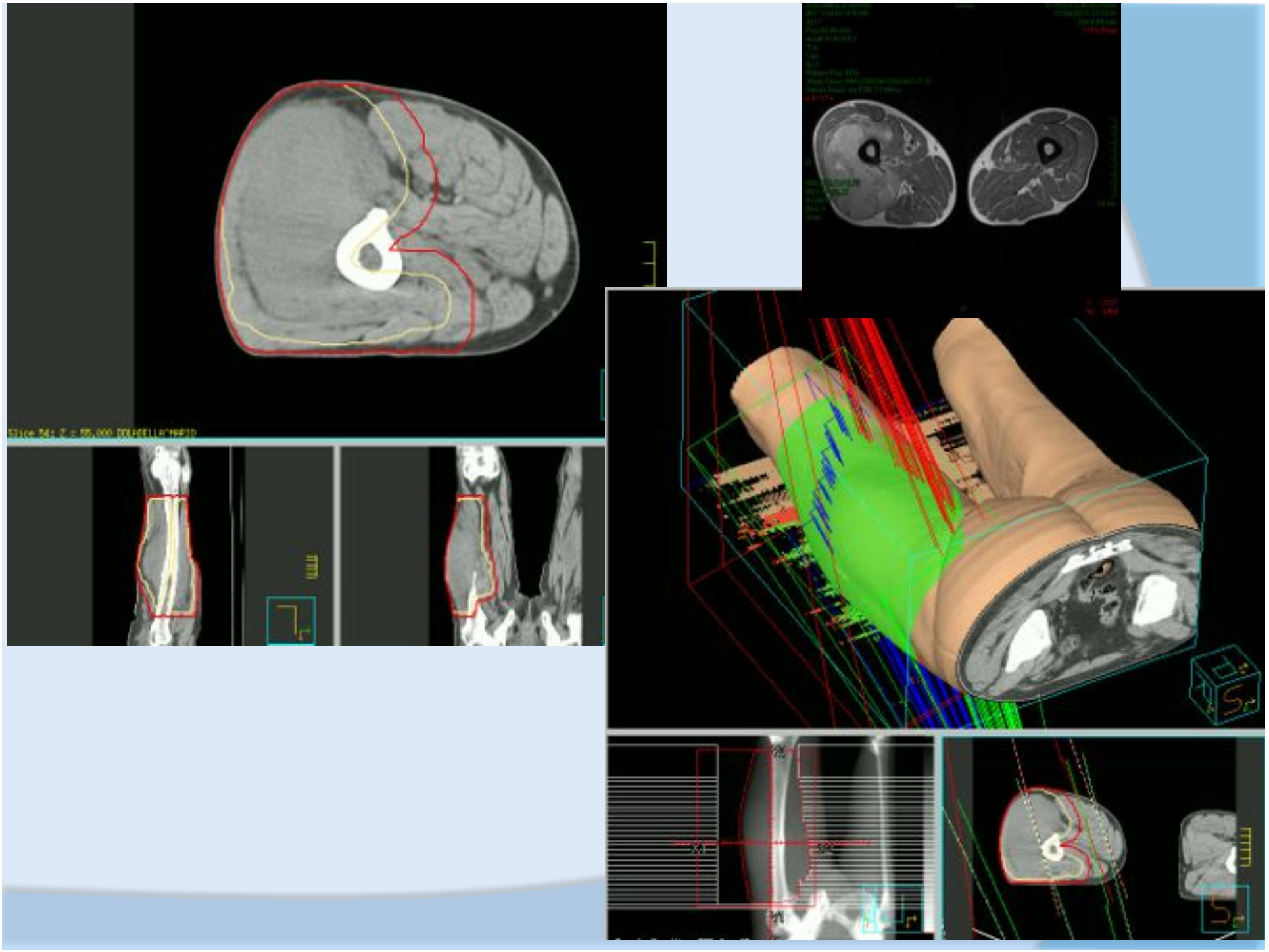
1 cm

isotropically



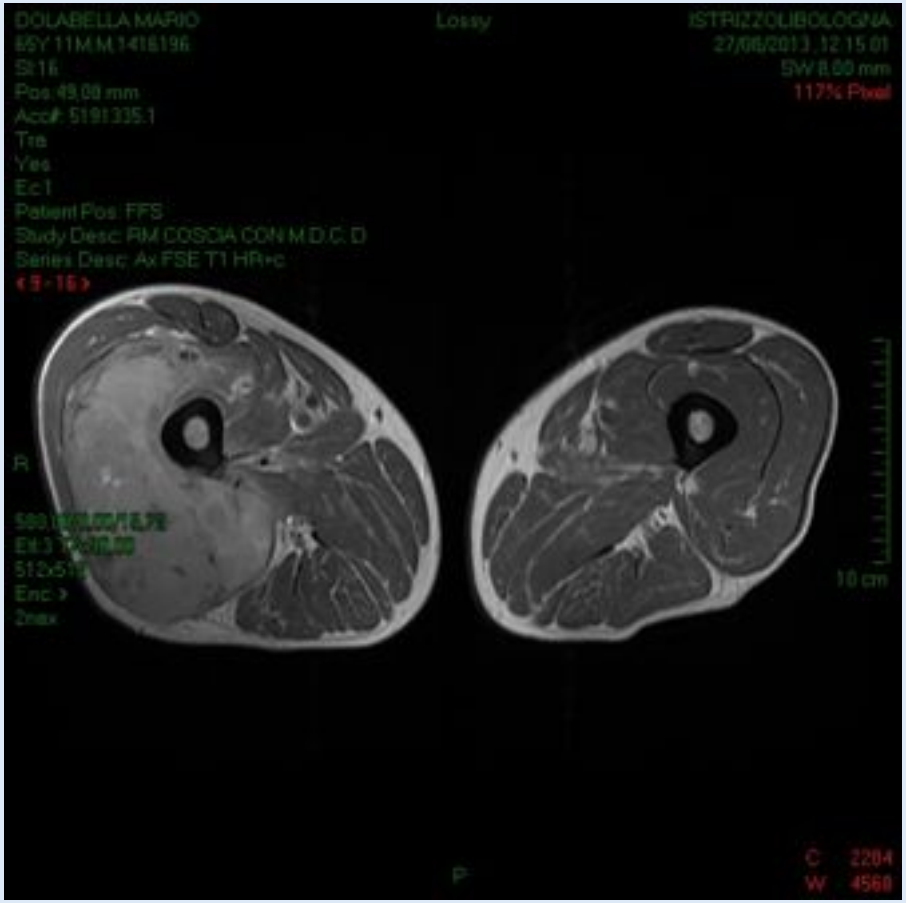
Fusion RMN pre-RTE/TC





Results....

RMN PRE-RTE



RMN POST-RTE/PRE-CHIRURGIA

Median reduction of the tumor volume: 25,4%

Results...

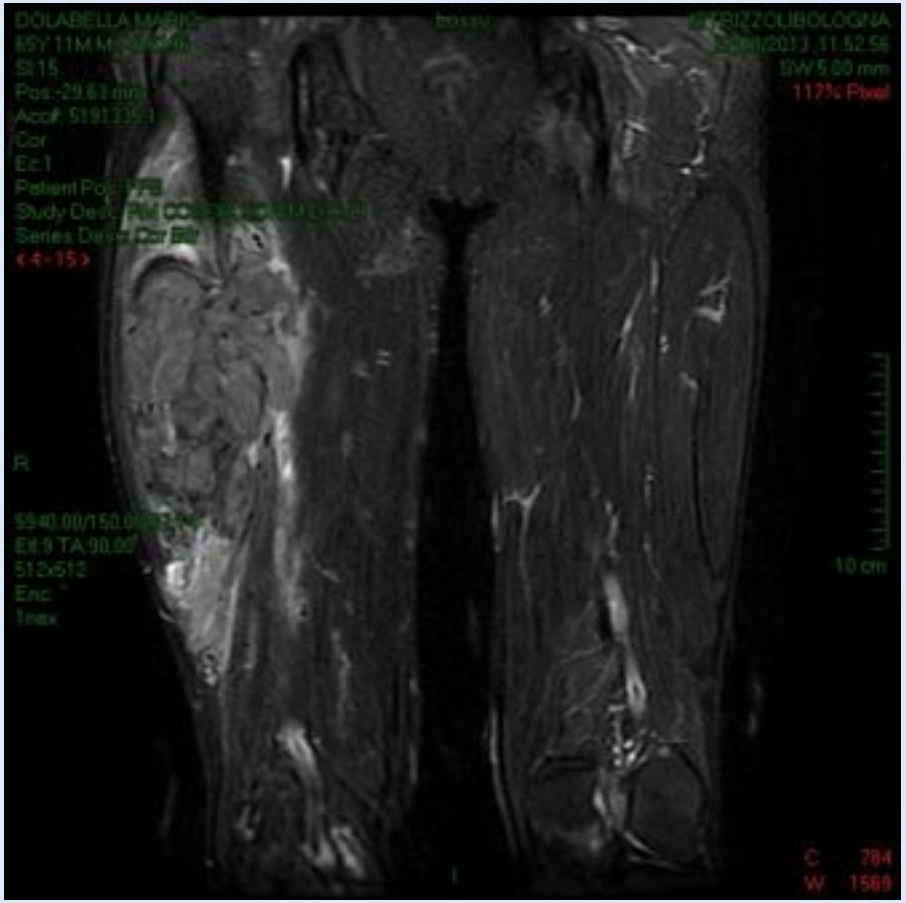
RMN PRE-RTE

RMN POST-RTE/PRE-CHIRURGIA

Median reduction of the tumor volume: 25,4%

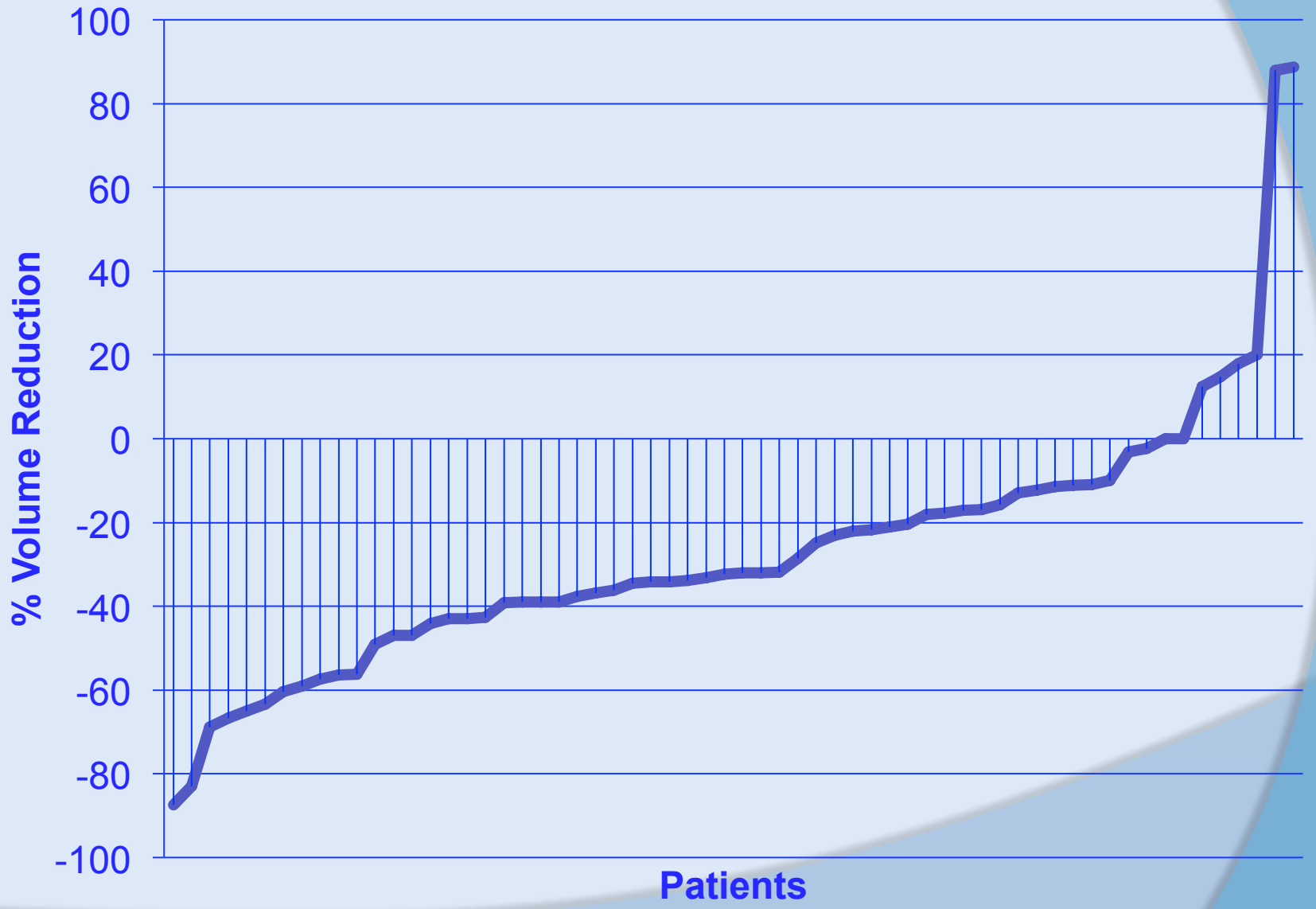
RMN PRE-RTE

RMN POST-RTE/PRE-CHIRURGIA

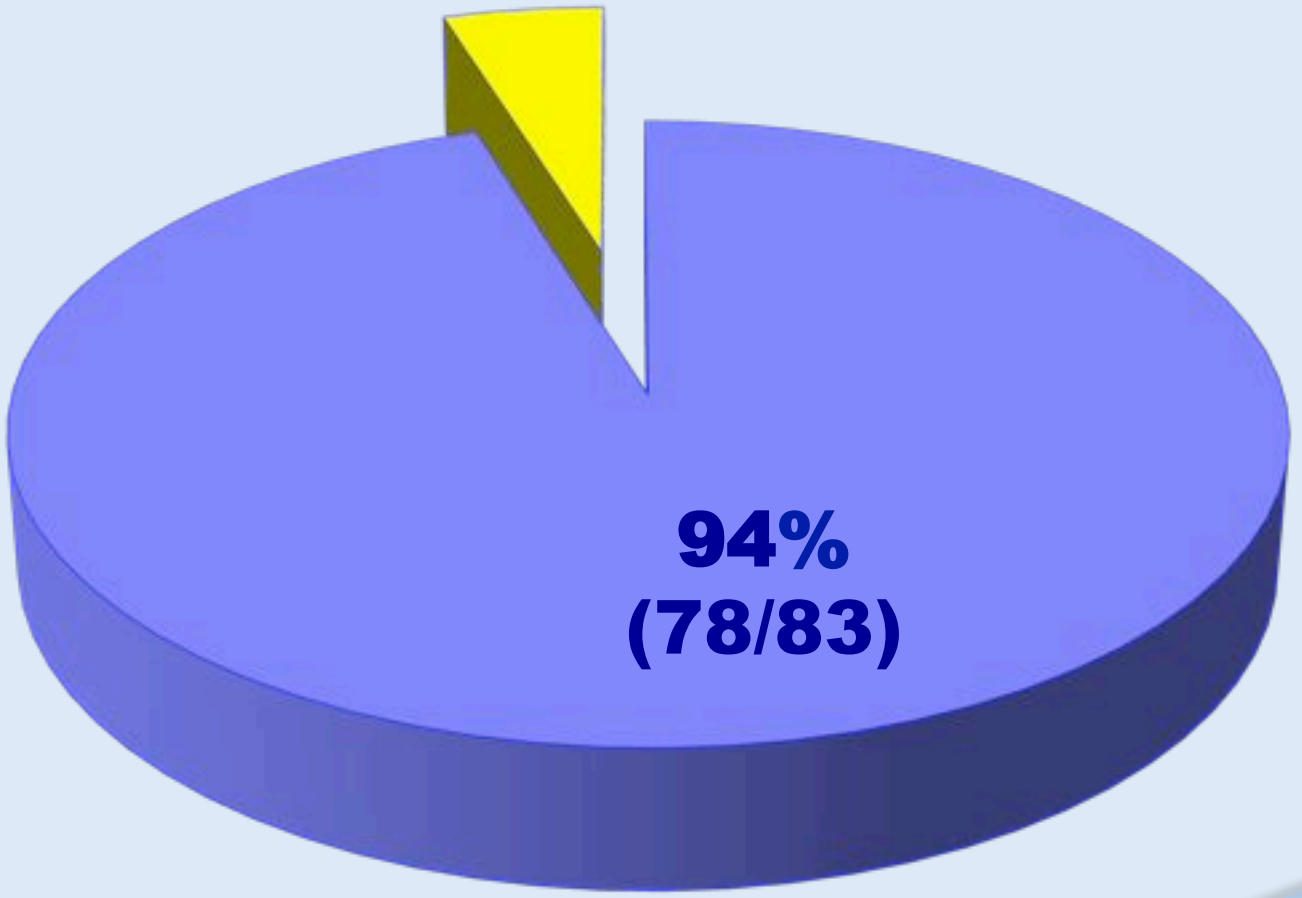


Median reduction of the tumor volume: 25,4%

Results



Results



Follow-up mediano: 45,7 mesi (9-87)

Results


86,7%
72/83
92,8%
77/83
96,4%
80/83
13,3%
11/83
6,6%
6/83
3,7%
3/83
Nr Patients
0
10
20
30
40
50
60
70
80
Linfedema
Deficit funzionale
Riduzione sensibilità
Diseases

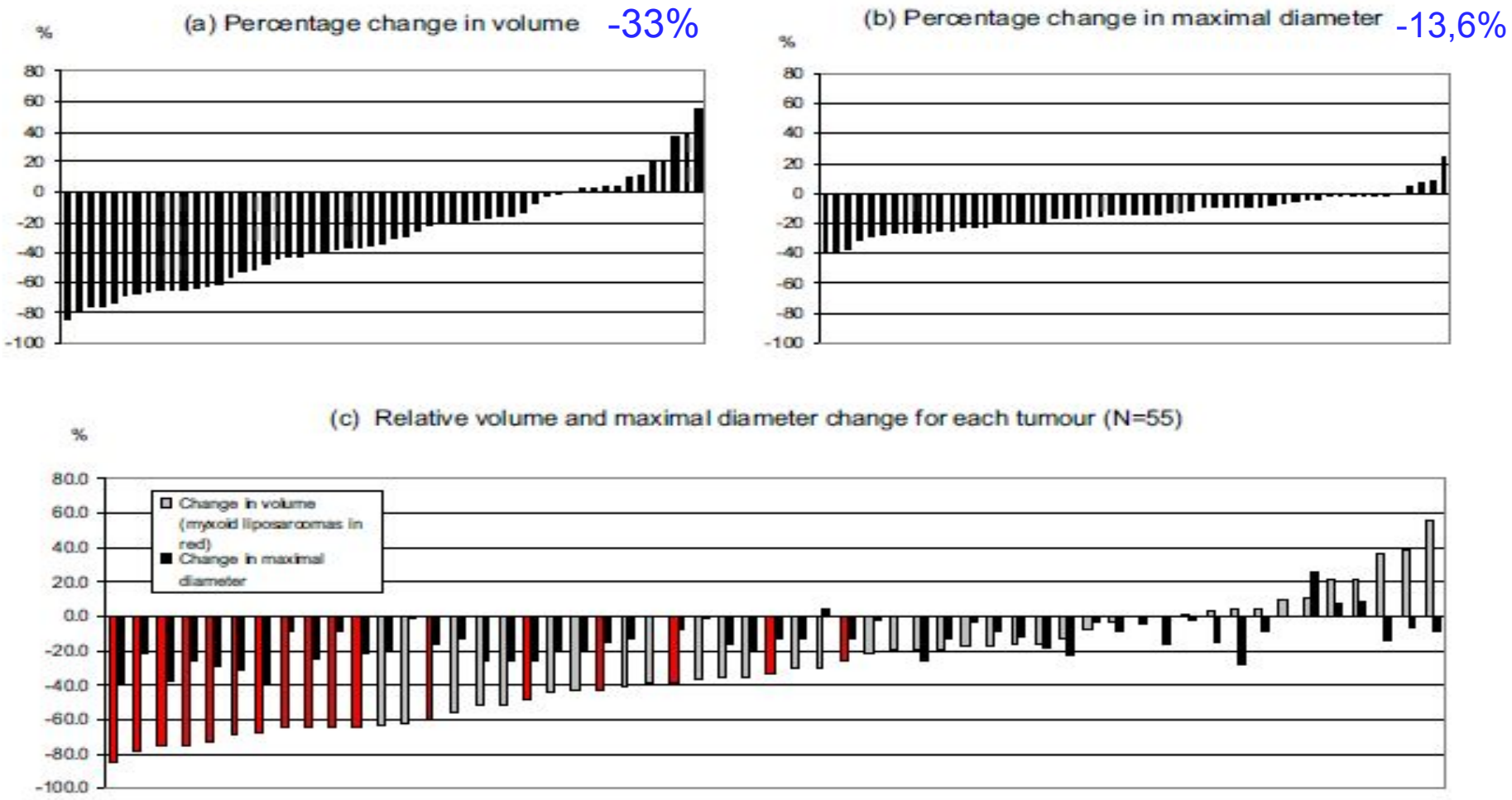
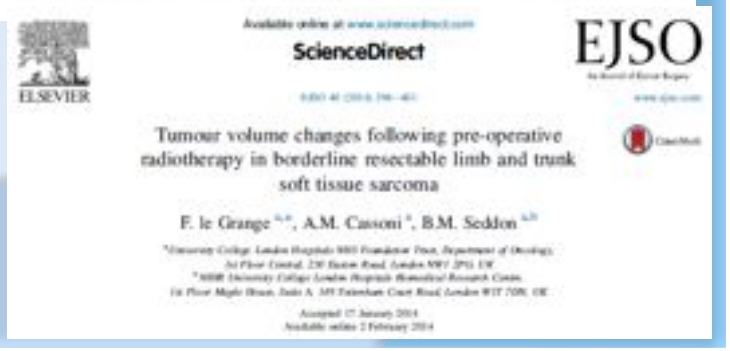


Figure 1. Percentage change in volume and maximal diameter. (a) The percentage change in volume for each tumour. (b) The percentage change in maximal diameter for each tumour. (c) The relative percentage change in maximal diameter and volume for each tumour with myxoid liposarcomas in red. ($N = 55$).



Conclusions

Effectiveness of neoadjuvant CHRT

- Reduction in the volume of tissue irradiated.
- Performance of more conservative surgery after tumor shrinkage
- Potentially leading to decreased late tissue morbidity.

Grazie a tutti per l'attenzione