Radiotherapy for Desmoids tumors

MP Sunyach

Modern technics allows to decreased dose delivered to the normal structure

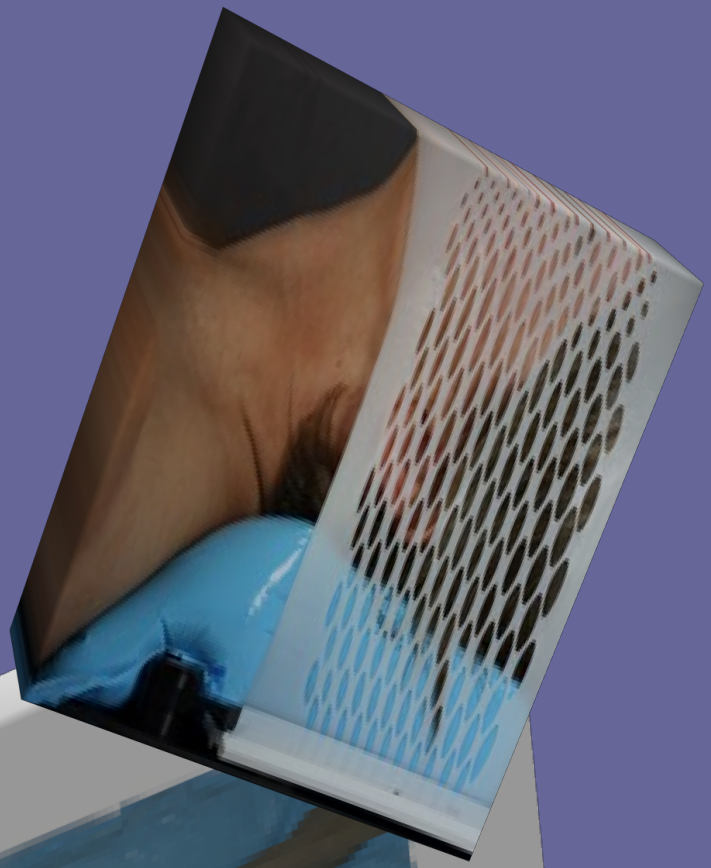
- Personnal immobilisation device
- Image Guided Radiotherapy :
  - Control before and during seance
- Precision of the dose distribution :
  - RC 3D
  - IMRT
  - VMAT

First stape SIMULATION

CT scanning for:

- spatial localisation of patient anatomy, including Organ At Risk and tumor contours

Immobilisation equipment



The second stape : PLANNING

3D planning takes into account the variations in dose distribution caused by heterogeneities (lung.... bones....)

. Current computers are able to compute dose in three dimensions

exemple

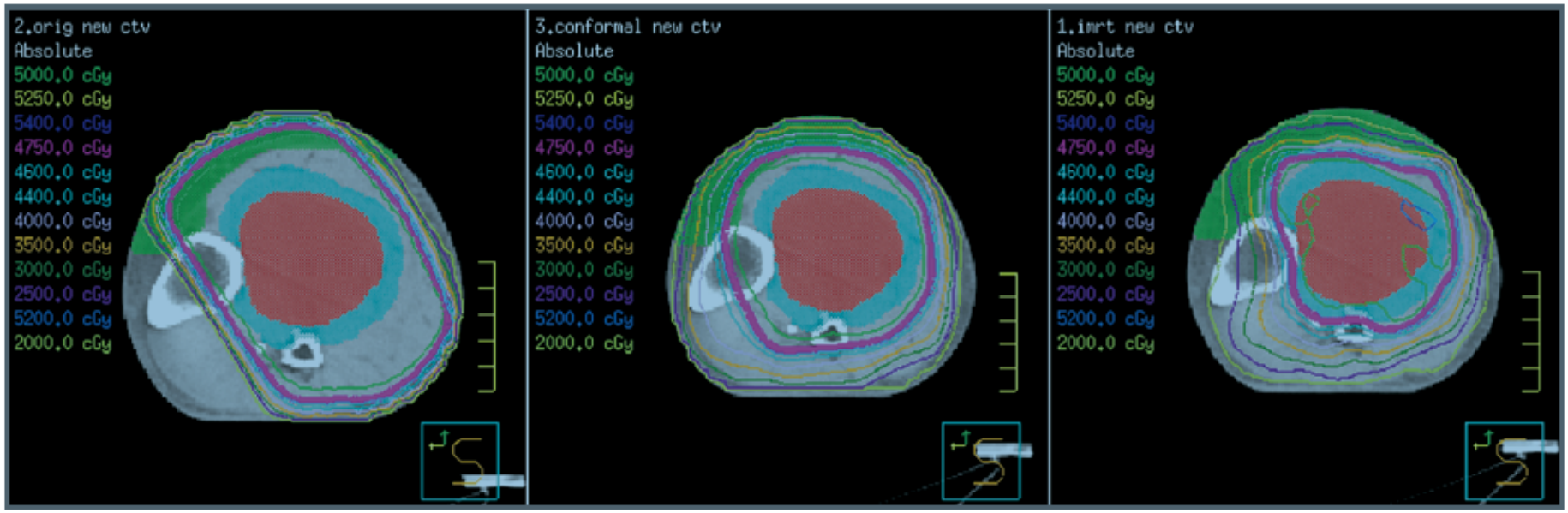
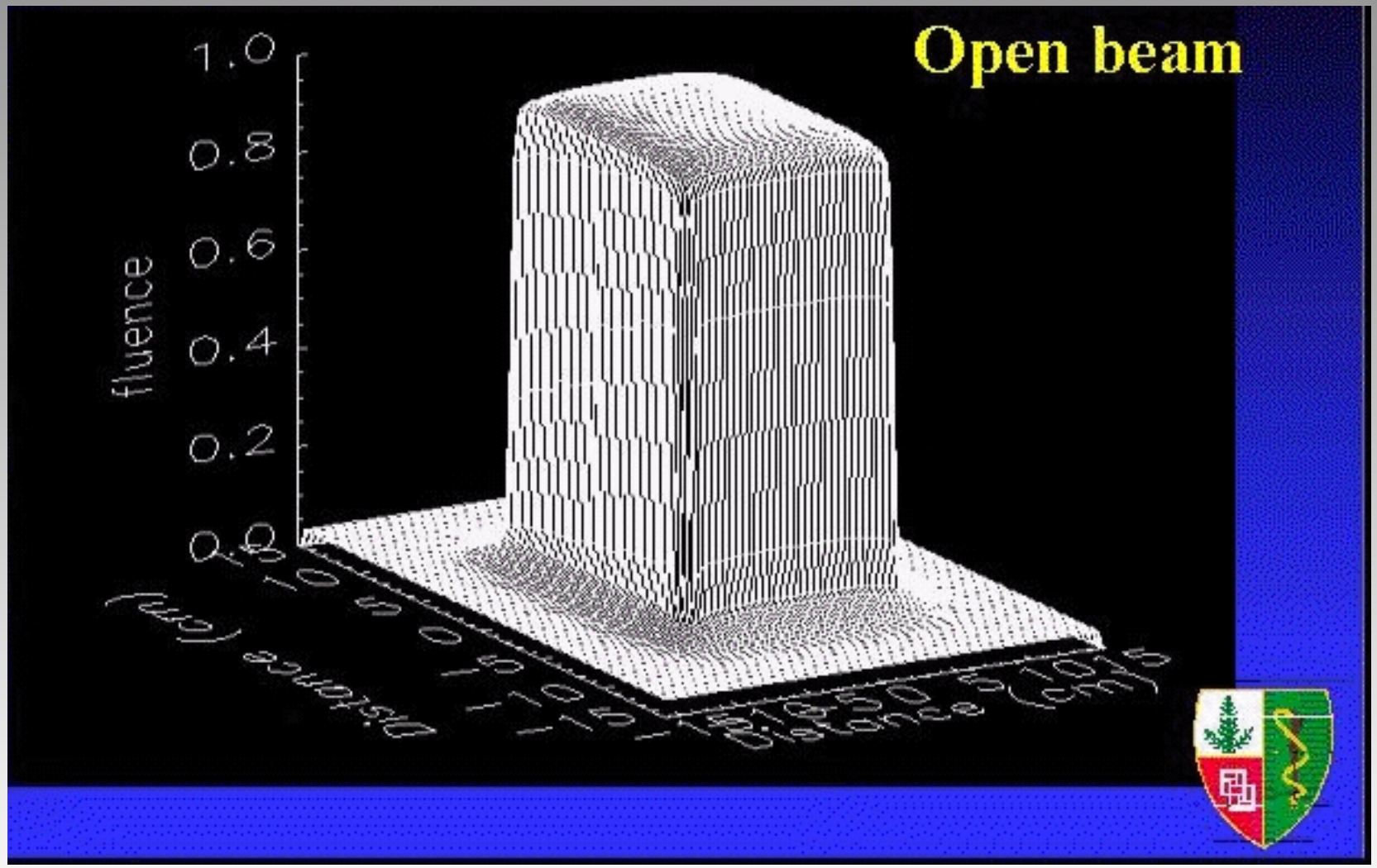
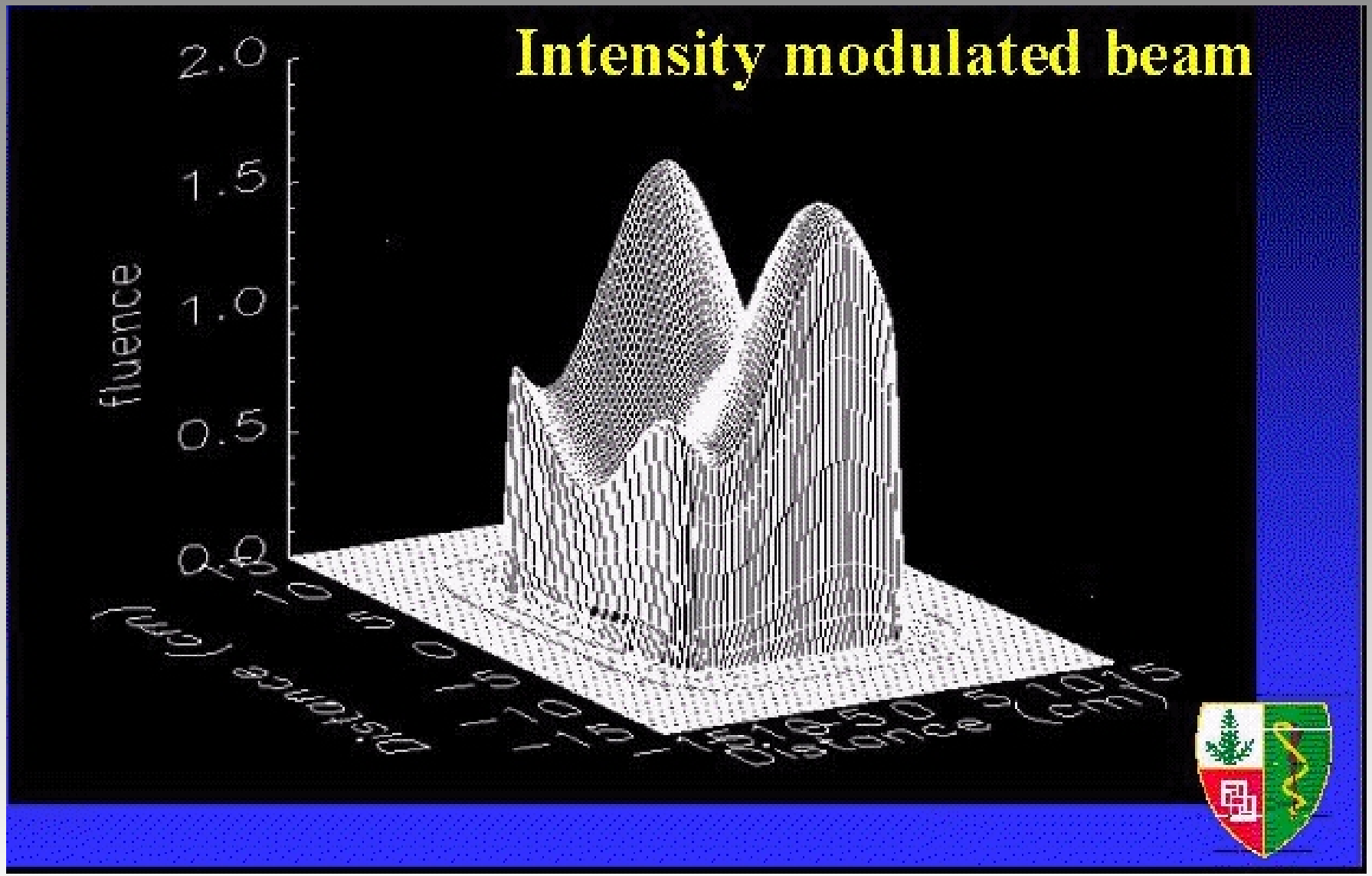


Fig. 4. Axial views demonstrating isodose displays for original, conformal, and intensity-modulated radiotherapy plans for Patient 8. Red color wash contour represents gross tumor volume; light blue color wash contour, clinical target volume; and green color wash contour in anterior leg, medial, and lateral flaps.

Beam with no modulation



IMRT

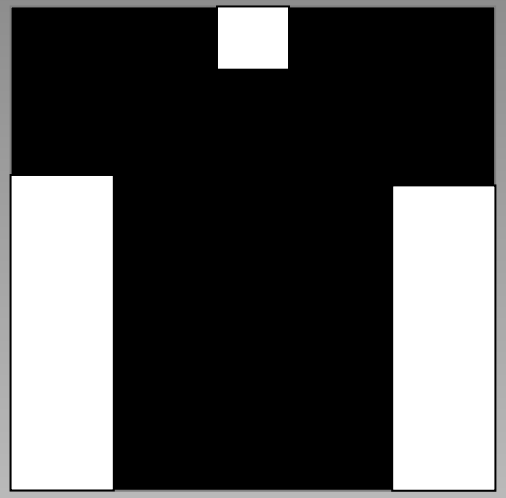


Principe of IMRT

3DRT:

-beam

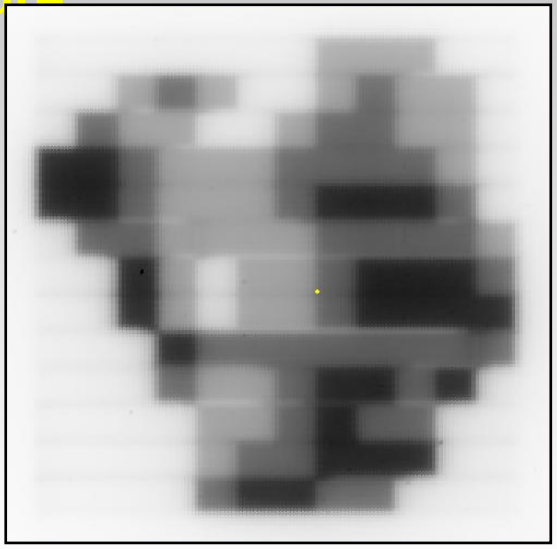
uniformedose



IMRT:

-

Complex dose distribution sparing critical structure



RC-3D exemple

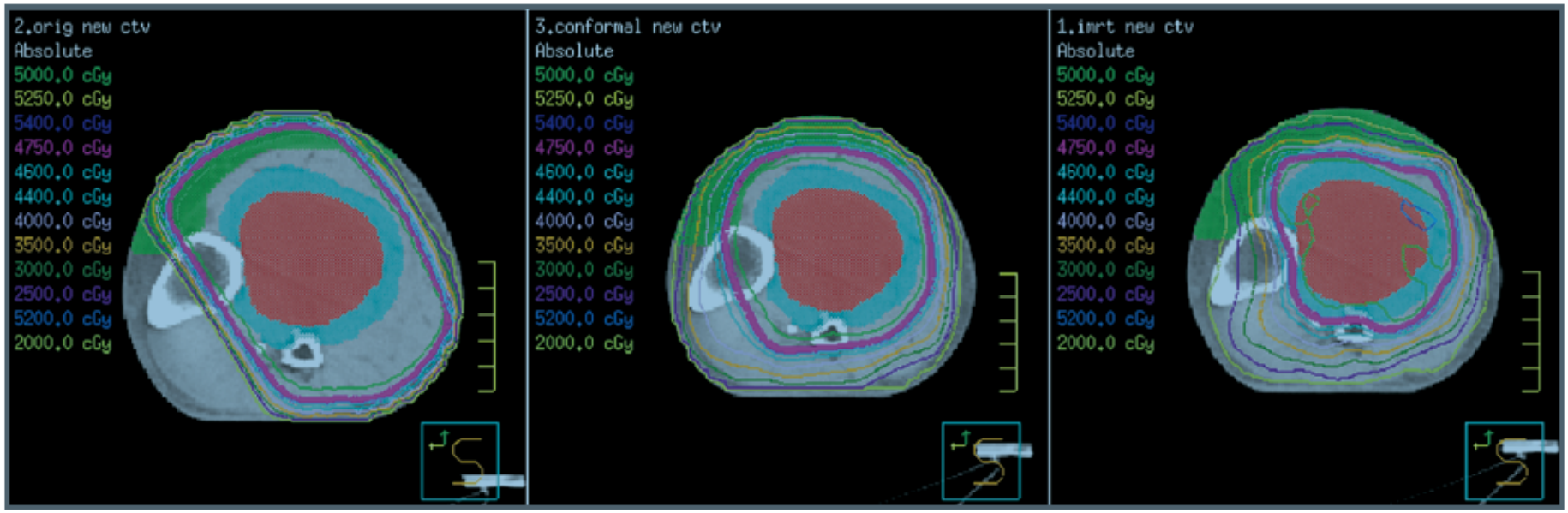
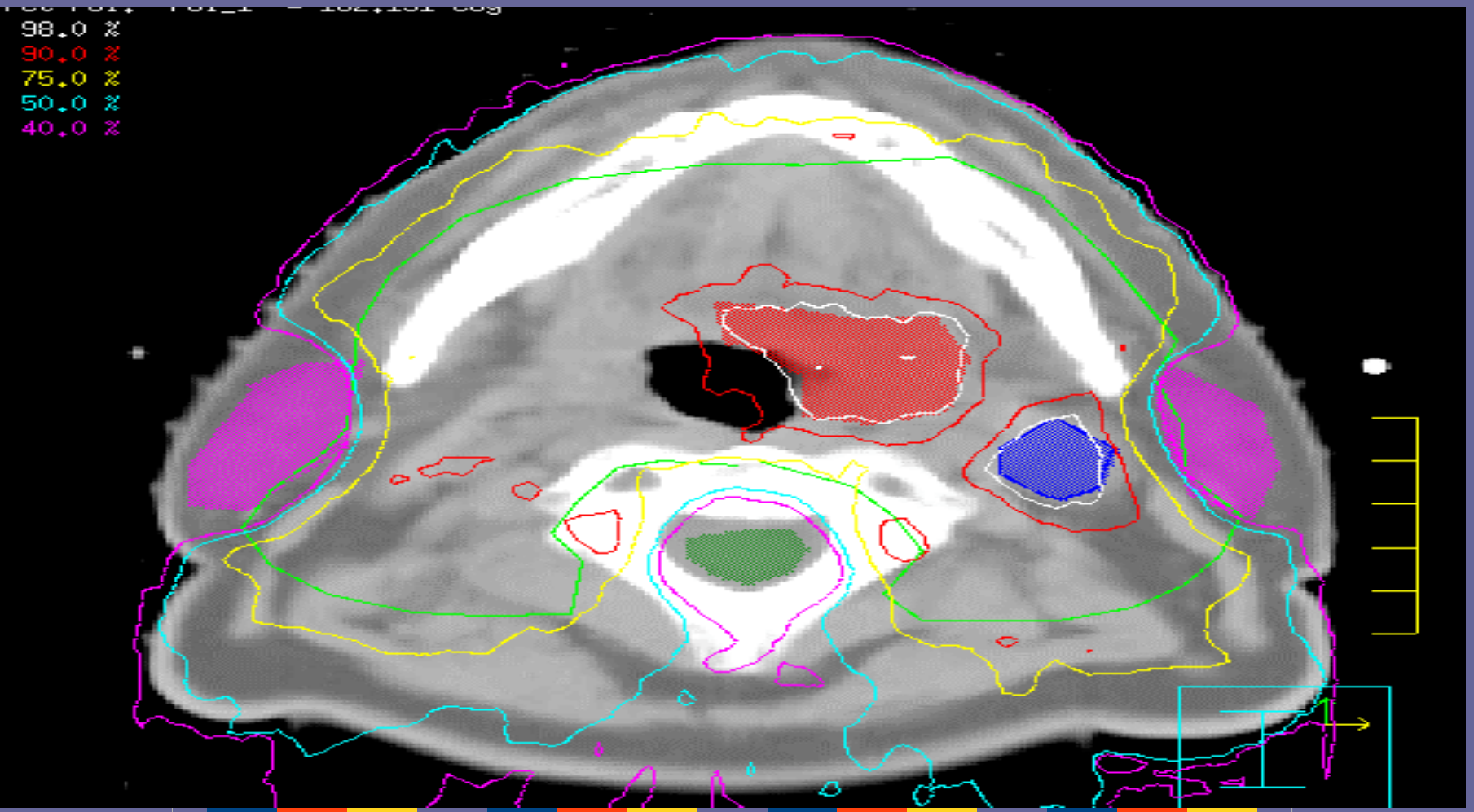
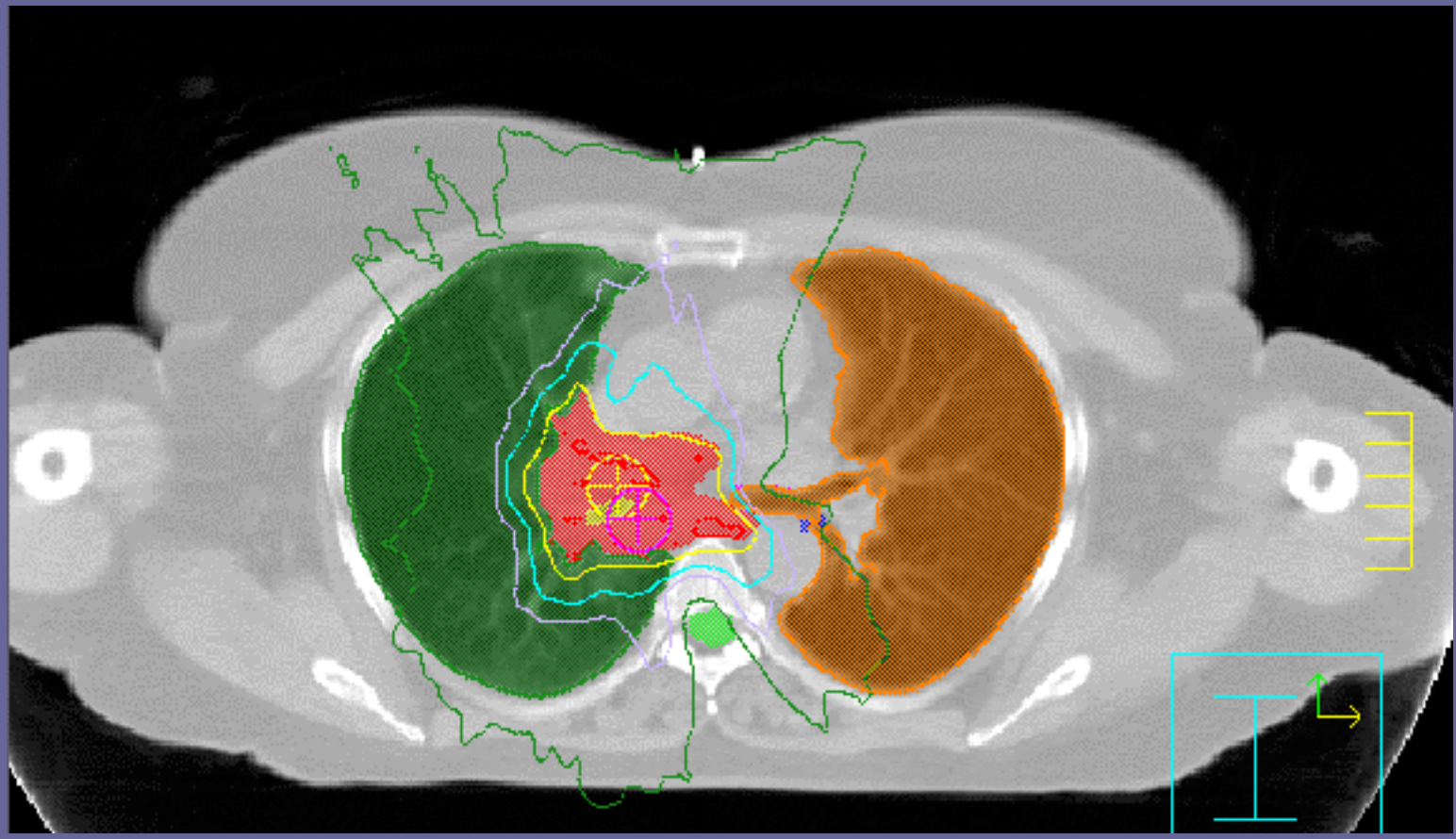
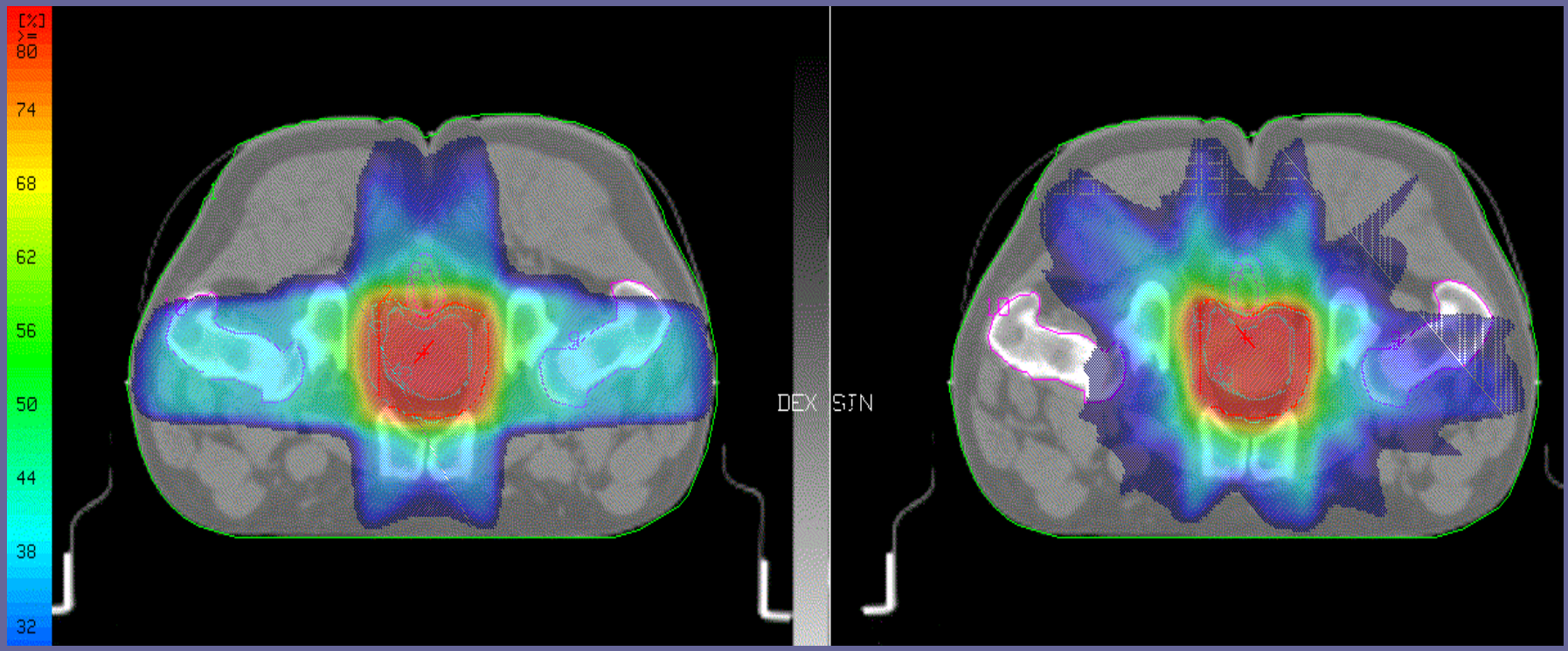


Fig. 4. Axial views demonstrating isodose displays for original, conformal, and intensity-modulated radiotherapy plans for Patient 8. Red color wash contour represents gross tumor volume; light blue color wash contour, clinical target volume; and green color wash contour in anterior leg, medial, and lateral flaps.

Dose to OAR spinal cord reduced






[%]
>=
80
74
68
62
56
50
44
38
32
DEX
SIN

The last stape TREATMENT

It is important to ensure that the tumour (and normal tissues) are where you think they are.

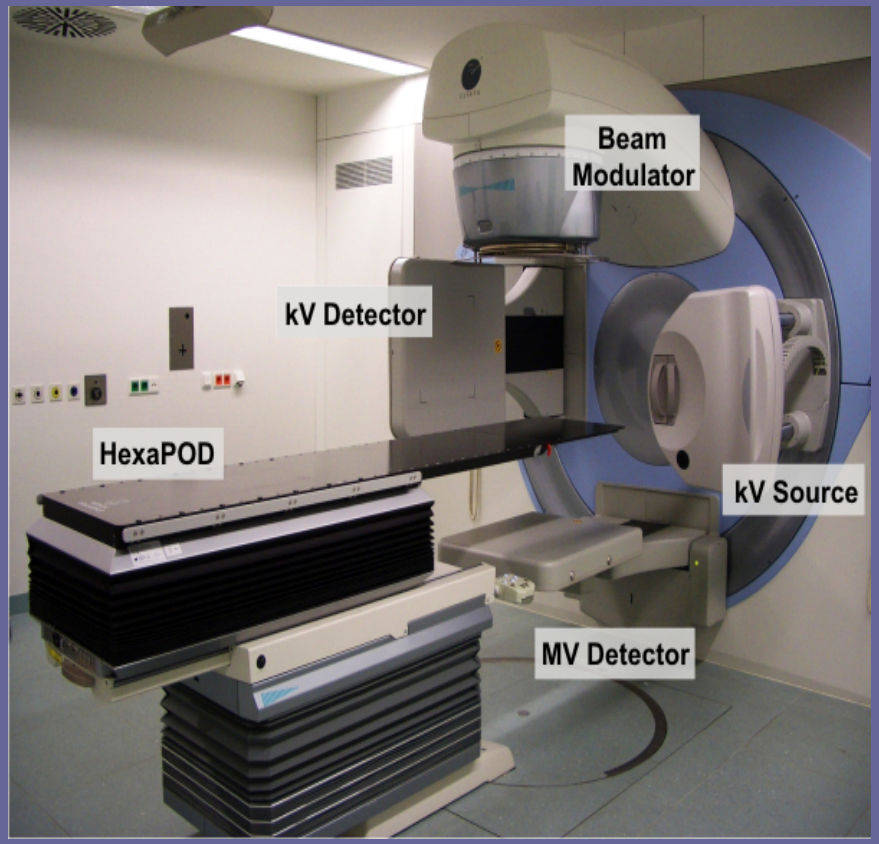
There is a balance between reducing margins to miss normal tissues versus sufficient margins to cover the disease volume

Checking the position

image acquisition prior to every treatment,

- with an on board imaging device,
- The target volume is identified and compared with the volume in planning.
- If significant deviation has occurred, the radiotherapy delivery may be mildly adjusted

Accelerator able to treat and control the position by imaging 3D



Accelerator able to treat and control the position by imaging 2D

What about

Desmoid tumors ????

Radiotherapy After surgery ?

Local failure after excision 25%-40%

No phase III Study =

– No certitude

South Carolina; 2000 (1983-1998) PMID 10738207 -- "Surgery versus radiation therapy for patients with aggressive fibromatosis or desmoid tumors: A comparative review of 22 articles." (Nuyttens JJ, Cancer. 2000 Apr 1;88(7):1517-23.)

Surgery versus Radiation Therapy for Patients with Aggressive Fibromatosis or Desmoid Tumors

A Comparative Review of 22 Articles

Joost J. Nuyttens, M.D.
Philip F. Rust, Ph.D.
Charles R. Thomas, Jr., M.D.
Andrew T. Turrisi III, M.D.

BACKGROUND. Desmoid tumors (aggressive fibromatoses) are benign neoplasms with high rates of recurrence after surgery. Radiotherapy is sometimes reported to prevent recurrences, but not in all studies. In order to evaluate the effect of radiation, comparative analysis was performed.

METHODS. The authors conducted a MEDLINE search and collected all articles in the English language on the treatment of "desmoid tumor" or "aggressive fibromatosis" from the years 1983–1998. They categorized treatment into three groups: surgery alone (S), surgery with radiotherapy (S + RT), or radiotherapy alone (RT). The S and S + RT groups were each subdivided according to whether margins were free (−), positive (+), or unknown. Each subgroup was divided into cases with primary, recurrent, or unknown tumor.

RESULTS. The local control rates after treatment for cases in the S group with (−) margins, (+) margins, and overall were 72%, 41%, and 61%, respectively. For the S + RT group the local control results were 94%, 75%, and 75%, respectively, significantly different when compared with the results for the S group. For the RT group, the local control was 78%, significantly superior to that of the S group (61%). Cases with primary and recurrent tumors had significantly superior local control rates with S + RT or RT versus S. Radiotherapy complications noted were fibrosis, paresthesias, edema, and fracture.

CONCLUSIONS. RT or S + RT results in significantly better local control than S. Even after dividing the groups into cases with free and positive margins and cases with primary and recurrent tumors, the best local control is achieved with RT or S + RT.
Cancer **2000;88:1517–23.**

KEYWORDS: desmoid tumor, aggressive fibromatosis, surgery, radiotherapy, complications.

Aggressive fibromatosis is a benign neoplasm that arises from fascial and musculoaponeurotic tissues. These tumors lack a capsule, infiltrate along fascial planes, and invade adjacent neurovascular structures.[1] Local recurrences may occur even after a wide resection. Some resections may be mutilating. Disfigurement may be avoided in some instances by radiotherapy, either alone or after conservative surgery, without compromise in local control. Radiotherapy has a relapse rate of 31% for unresectable tumors.[2] There seems to be evidence that radiotherapy is helpful in the management of aggressive fibromatosis, although the role and precise indication for this modality has not been defined clearly. In an attempt to put the multimodal management of the desmoid tumor in some perspective, a comparative review of 22 articles regarding the roles of surgical and radiotherapy for aggressive fibromatosis was performed.

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Received August 26, 1999; revision received November 22, 1999; accepted November 22, 1999.

South Carolina; 2000 (1983-1998) PMID 10738207 -- "Surgery versus radiation therapy for patients with aggressive fibromatosis or desmoid tumors: A comparative review of 22 articles." (Nuyttens JJ, Cancer. 2000 Apr 1;88(7):1517-23.)

Publications 83-98.

22 articles

718 pts

FU: 6 y.

South Carolina; 2000 (1983-1998) PMID 10738207 -- "Surgery versus radiation therapy for patients with aggressive fibromatosis or desmoid tumors: A comparative review of 22 articles." (Nuyttens JJ, Cancer. 2000 Apr 1;88(7):1517-23.)

RESULTS : Local control

surgery 61%

Surgery + RT 75%

RT alone 78%

Toxicity: RT complications fibrosis, paresthesias, edema, fractures

Conclusion: RT or surgery + RT results in significantly better local control than surgery alone

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RTE is effectiv after surgery R1 and R0

TABLE 3
Local Control for Free Margins, Positive Margins, or Unknown Margins Treated with Surgery Alone, Surgery with Radiotherapy, or Radiotherapy Alone

	Surgery alone		Surgery + RT			RT alone[a]		
	No.	%	No.	%	*P* value[b]	No.	%	*P* value
Free margins	171/237	72	33/35	94	0.0048			
Positive margins	50/121	41	174/232	75	4×10^{-10}	80/102	78	NA
Unknown margins	13/23	56	14/26	54	NA			
Total	234/381	61	223/297	75	0.0002	80/102	78	0.023

RT: radiotherapy; No.: number of patients with local control, NA: not available.
[a]All patients treated with radiotherapy alone had macroscopic disease.
[b]*P* value in comparison with surgery alone.

The impact of radiotherapy in the treatment of desmoid tumours. An international survey of 110 patients. A study of the Rare Cancer Network

Brigitta G Baumert*[1,2], Martin O Spahr[1], Arthur Von Hochstetter[3], Sylvie Beauvois[4,25], Christine Landmann[5], Katrin Fridrich[6,24], Salvador Villà[7], Michael J Kirschner[8,22], Guy Storme[9], Peter Thum[10], Hans K Streuli[11], Norbert Lombriser[12], Robert Maurer[13], Gerhard Ries[14], Ernst-Arnold Bleher[15], Alfred Willi[16], Juerg Allemann[17], Ulrich Buehler[18], Hugo Blessing[19,26], Urs M Luetolf[1], J Bernard Davis[1], Burkhardt Seifert[20] and Manfred Infanger[2]

An international study of Rare Cancer Networkthe
110 patients
, the addition
of radiation therapy after surgery was an independent positive prognostic factor for local recurrence and overall survival

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Results : Recurrences :

- Post surgical E RT :17/ 68 patients (25%)
- Surgery alone : 12/38 patients(32%)

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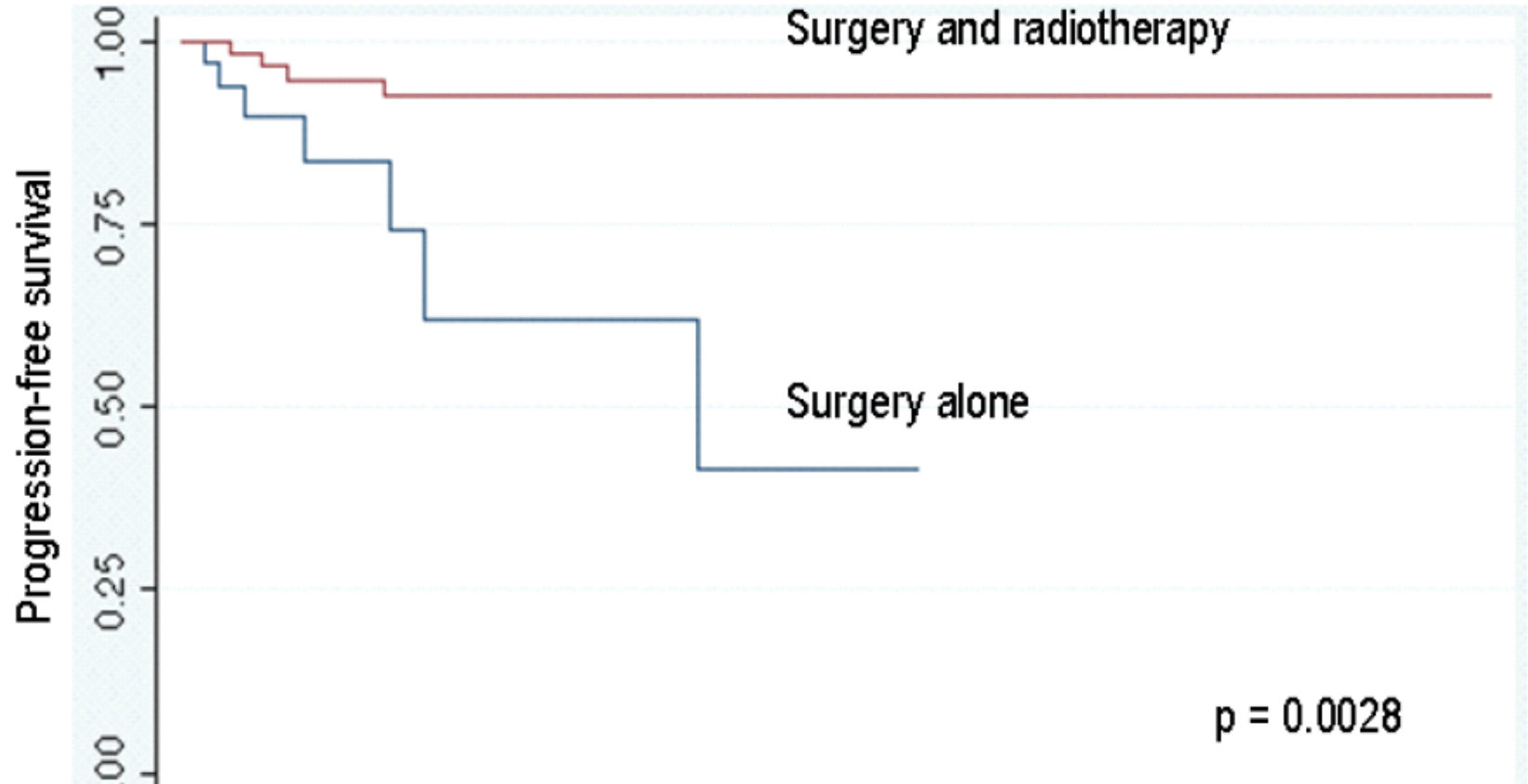

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Group EBRT : Recurrences were seen :

at the field borders in7 cases

within the field in 10 cases.

in areas where the dose was less than 50 Gy in 65 % of case.

Conclusion of the author is

Dose at least of 50 Gy has to be delivered

Field margin has to be at least 5 cm.

But no value prognostic value for surgical margin

-
  - Gronchi, A., et al. "Quality of surgery and outcome in extra-abdominal aggressive fibromatosis: a series of patients surgically treated at a single institution." J.Clin.Oncol. 21.7 (2003): 1390-97.
  - Merchant, N. B., et al. "Extremity and trunk desmoid tumors: a multifactorial analysis of outcome." Cancer 86.10 (1999): 2045-52.
  - Bonvalot, S., et al. "Extra-abdominal primary fibromatosis: Aggressive management could be avoided in a subgroup of patients." Eur.J.Surg.Oncol. 34.4 (2008): 462-68.

Loocking for relevant prognostic factor

To select patients who need post operativ radiation therapy

AGE ? Tumor site ?

Beta cathenine ?

News factors ?

Curative or exclusive EBRT

Are demsmoid tumor radiosensitiv ?

Exclusive RT

- littérature……

- Zlotecki, R. A., et al. "External beam radiotherapy for primary and adjuvant management of aggressive fibromatosis." Int.J.Radiat.Oncol.Biol.Phys. 54.1 (2002): 177-81.
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- El-Haddad, M., et al. "Treatment of aggressive fibromatosis: the experience of a single institution." Clin.Oncol.(R.Coll.Radiol.) 21.10 (2009): 775-80.
- Gluck, I., et al. "Role of radiotherapy in the management of desmoid tumors." Int.J.Radiat.Oncol.Biol.Phys. 80.3 (2011): 787-92.
- Nuyttens, J. J., et al. "Surgery versus radiation therapy for patients with aggressive fibromatosis or desmoid tumors: A comparative review of 22 articles." Cancer 88.7 (2000): 1517-23.

	n	Local control	Doses RT	Site orcf recurrence.
(Gluck et al. 787-92)Michighan 1984 200 95 pts 8-87ans	13	3 y : 92.3%		In field :5pts 3
(Rutenberg et al.)1978 2008 30pts 8-30 ans	15	15 ay67%	55-65 Gy	ne
(Zlotecki et al. 177-81) 1975-2000 65 pts 10-78 ans	32	5 y78%	50-54 Gy	In field : 2pts Fields margins 9
(Micke and Seegenschmiedt 882-91) 112 institutions 1976 345 pts	204	81 %	36-65 Gy	ne
(Baumert et al. 12)	0	ne	ne	61 % fields margins
(El-Haddad et al. 775-80) 1990 2006 AS 54 pts 2-63 ans	0	ne	45 - 60 Gy	

	TTT	age	Site t	size	margin	PFactors
, (Rutenberg et al.) 1978 2008 30pts 8-30 ans	NS	NS	NS	NS	NS	Dose 55 gy rec.
(Gluck et al. 787-92) Michighan 1984 2004 95 pts 8-87ans	NS	NE	0.035	NS	NS	
(Zlotecki et al. 177-81) 1975-2000 65 pts 10-78 ans	NS	NE	NE	NE	NS	Rec
(Micke and Seegenschmiedt 882-91) 112 institutions 1976 345 pts	NS	NE	NS	NS	NS	Rec 0.08
(Baumert et al. 12) NE/SU/NO BE/ES 110 pts 1-78 ans	NS	NS	0.01 Abdo péjoratif	NE	NS	Dose>50 Gy
(El-Haddad et al. 775-80)	NS	NE	0.010	NS	NS	Sexe 0.010

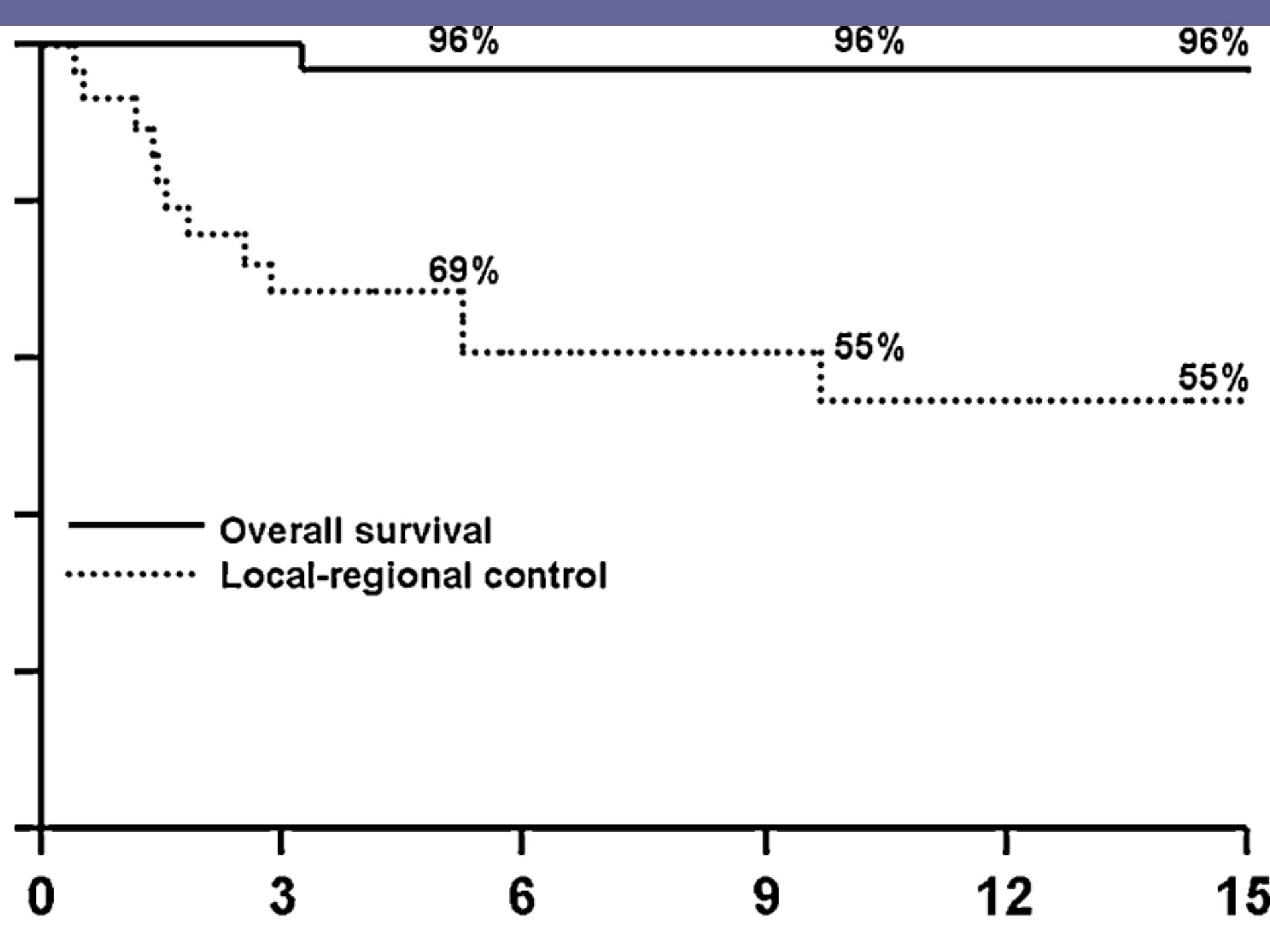
	recurrence	FU	TTT	Local control	Toxicity
(Gluck et al. 787-92) Michigan 1984 2004 95 pts 8-87ans	23/95	38 ms	surgey :54pts surgery+rte :28pts Rte :13pts	3 y 84.6% 69% 92.3%	1 décès evol / polypose Second cancer 1 stomac 1 osteonecrose 3 fonctionnal
(Rutenberg et al.) 1978 2008 30pts 8-30 ans	NE	13 y	surgery :14pts Rte :15pts surgery+rte :1pts	15 y 53 % 67%	3fractures
(Zlotecki et al. 177-81) 1975-2000 65 pts 10-78 ans	42/65	6 y	Xie+rte :32pts Rte : 33pts	5 y 78% 87%	3/65 fractures
(Micke and Seegenschmiedt 882-91) 112 institutions 1976 345 pts	50% >2 xie	43 ms	Xie +rte :141pts Rte :204pts	81% 79,6%	No second cancer
(Baumert et al. 12)		6 y	Xie +rte : 68 surgery :42pts Rte :0 pts	10 y 93 % 62%	No second cancer 4 sever bowel injuries
(El-Haddad et al. 775-80) 1990 2006 AS 54 pts 2-63 ans	28 rec. /54	7.3 y	surgery+rte :54 pts	10 y 67 %	No second cancer

toxicities

- 3 second cancers / 1322 pts
- Résultats satisfaisants même en récidive
- Nombreuses complications de la RTE en particuliers douleurs et troubles fonctionnels

RT for desmoid

- Larges volumes
- Dose 50-55 Gy


96%
96%
96%
69%
55%
55%
Overall survival
Local-regional control
0
3
6
9
12
15

Expérience CLB

- Expérience CLB

	Rec	Dose Gy	fu	DN réponse	douleurs
Pte1	oui	56	5A	Rp :60-40 mm	N0N
Pt2	oui	56	7A	RP	OUI
Pt3	oui	56	8A	RC	NON
Pt4	oui	56	4A	PR champ	OUI
Pt5	oui	54	6A	RC	OUI
Pt6	oui	56	8A	PR bordure	OUI
Pt 7	oui	56	4A	RP :96-60mm	NON mieux
Pt 8	oui	56	4A	PR bordure	NON
Pt 9	oui	56	3A	RP	NON
Pt 10	oui	56	3A	RP 78-40 mm	NON

conclusion

- Not always efficient for dolor….
- Tumor regression after several years
- Marginal recurrence

To evaluate the efficacy of radiotherapy for inoperable desmoid tumors, the Soft Tissue and Bone Sarcoma Group of the European Organization for Research and Treatment of Cancer (EORTC) performed a pilot study (EORTC 62991)

- assessing moderate-dose radiotherapy for aggressive
- fibromatosis in patients not amenable to resection
- without significant function loss. Patients received radiotherapy
- for a total of 56 Gy in 28 fractions. This nonrandomized,
- phase II study finalized recruitment with 44
- patients in April 2008, and patients are still under followup; the final analysis is awaited after 3 years of follow-up in
- the second quarter of 2011.

Toxicities

- Bones fractures
  - Reduced by modern RT
- Fibrosis necrosis
  - Reduced by modern RT
- Second cancer
  - ????
  - Low risk
  - Very long term risk
  - Probably not reduced by modern radiotherapy
  -

Observation before radiation

They may grow progressively larger over time, but growth is indolent, and periods of growth arrest are not uncommon

Medical treatment need 24 months to induced responce

When it may be proposed?

In case of evolutiv inoperable symptomatics disease ?

- Abdominal
  - New IMRT and VMAT
  - gaves news possibilities in selectiv case

- Appendix head and neck or parietal
  - For evolutiv symptomatics disease after failure of medical treatment

After surgery
Lack of selections criteria
Recurrence with second R2 resection and

Role for postop RT is not clear ;

It is currently not recommended for R1 resection,

It may be offered for R2 resection, particularly if there are concerns about local disease progression and morbidity/mortality

Why irradiated ?

To preserved the quality of life

Decreased dolor

Preserved function

Increased local control after surgery

Conclusion

- Desmoid tumors are a challenging clinical condition with locally aggressive behavior and a strong tendency for recurrence.

- Management options include :
  - observation, surgical resection,radiotherapy, conventional chemotherapy,hormonal agents, and newer moleculartargeted agents. A multidisciplinary approach
- tailored to the individual patient is
- usually needed, depending on the location,
- local effects, and clinical course.