Sarcoma Patients EuroNet

Radiotherapy for desmoids

Rick Haas,
Dept. of Radiotherapy
the Netherlands Cancer Institute – Amsterdam
the Leiden University Medical Center

EURACAN
European network for Rare adult solid Cancer

LUMC Leiden University Medical Center

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK

DISCLOSURES

Investigator Initiated Research Grants and Advisory Board Grants from

GSK
Novartis
Nanobiotix Company
PharmaMar
Lilly
Springworks Therapeutics

WHAT ARE DESMOIDS?

Synonyms:
- desmoid tumor
- desmoid fibromatosis
- aggressive fibromatosis

Desmoids are rare:
- ~0.03% of all neoplasms
- <3% of all soft tissue tumors
- 2–4 new cases per million per year

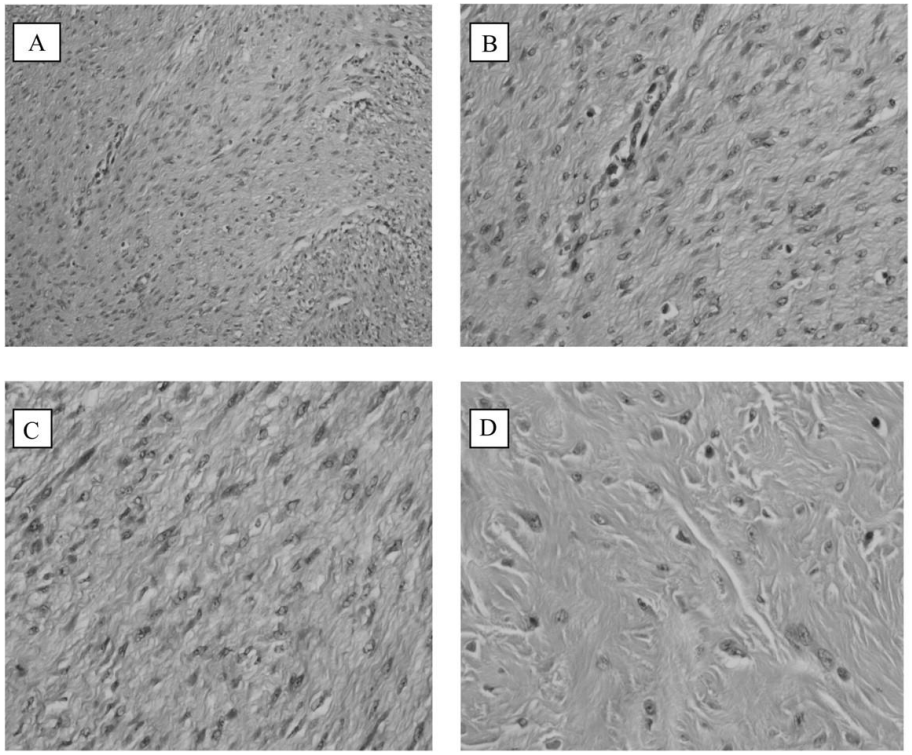
WHAT ARE DESMOIDS?

Types:

- Spontaneous (>90%)
  - mainly extremities and abdominal wall, but can be seen anywhere
- Associated with FAP (Gardner syndrome; 5-10%)
- Familial infiltrative fibromatosis, hereditary desmoid disease (~1%)
  - extremely rare, associated with APC mutations

PATHOLOGY CAN BE DIFFICULT

May look like scars



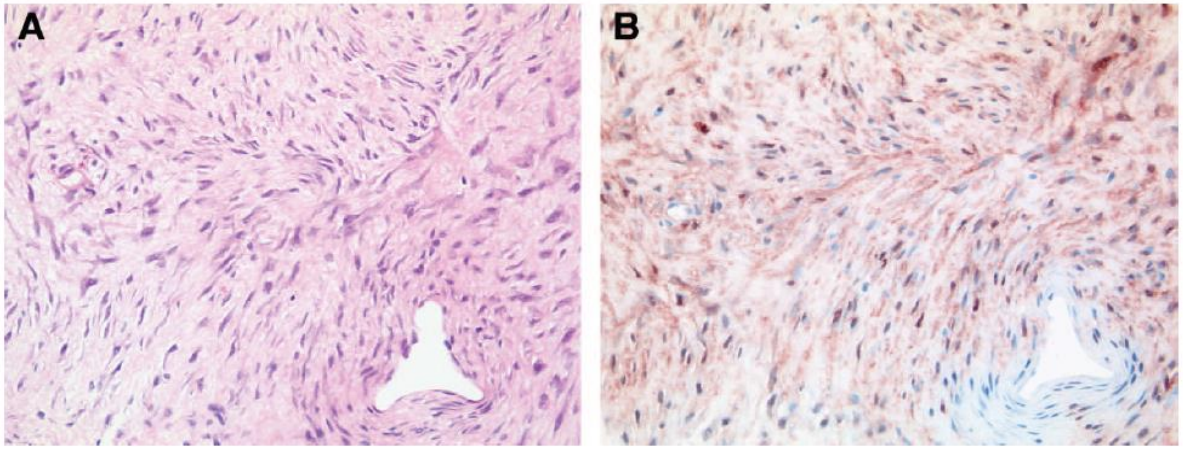
Escobar C et al. Ann Oncol 2012;23:562-569

Annals of Oncology

PATHOLOGY CAN BE DIFFICULT

Tumors are usually beta-catenin positive
mutations in codon 45F are associated with a worse prognosis

Many more chromosomal changes have been documented.



(A) Classic fibroblastic, spindle cell morphology of a desmoid tumor (hematoxylin and eosin, x200); **(B)** desmoid tumor with the characteristic expression of β-catenin (endothelial cells as negative control, x200).

WHAT IS A “TYPICAL” DESMOID PATIENT

Slightly more females than males
might be related to pregnancy (abdominal wall) and traumas

Typically between 10 and 40 years of age

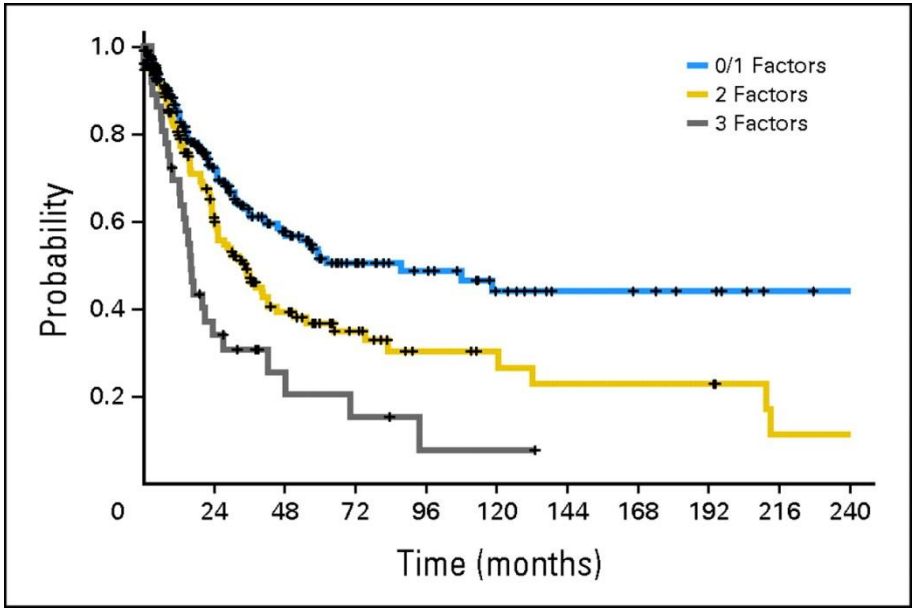
Usually a painless lump

Phases of growth and progression, stabilization, and sometimes spontaneous regression

It never metastasizes, but it may recur locally.

PROGNOSTIC FACTORS

Age <37 years
Size > 7cm
Extra-abdominal disease
Macroscopic residual disease after surgery

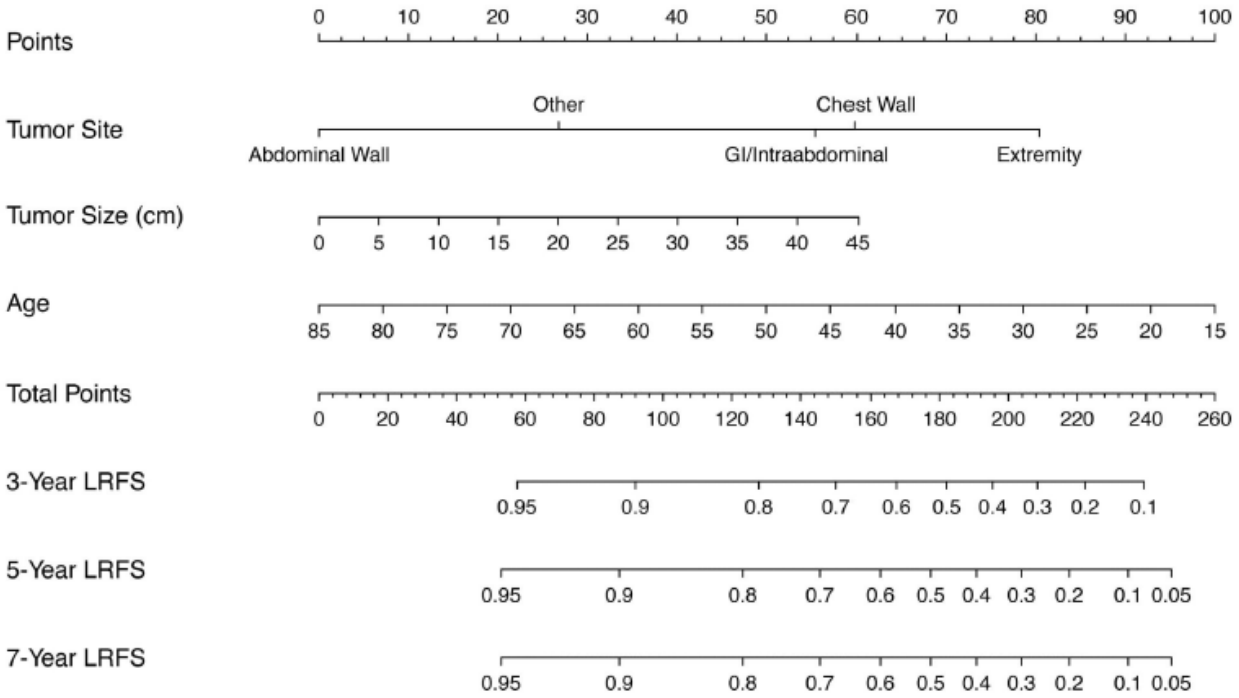


Salas S et al. JCO 2011;29:3553-3558

JOURNAL OF CLINICAL ONCOLOGY

PROGNOSTIC FACTORS

Size, site and age



Crago AM et al. Ann Surg 2013;258:347-53.

RT FOR DESMOIDS

Do nothing as long as reasonably possible

Weigh the balance between the trauma of therapy and the progression of the disease.

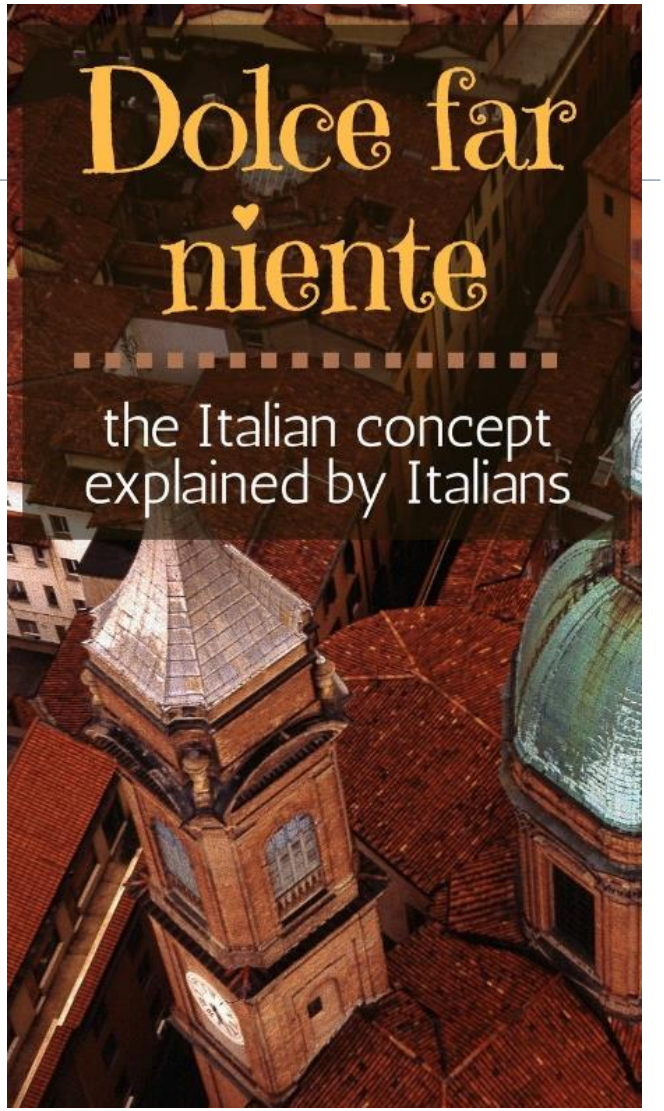
RT FOR DESMOIDS

Do nothing as long as reasonably possible

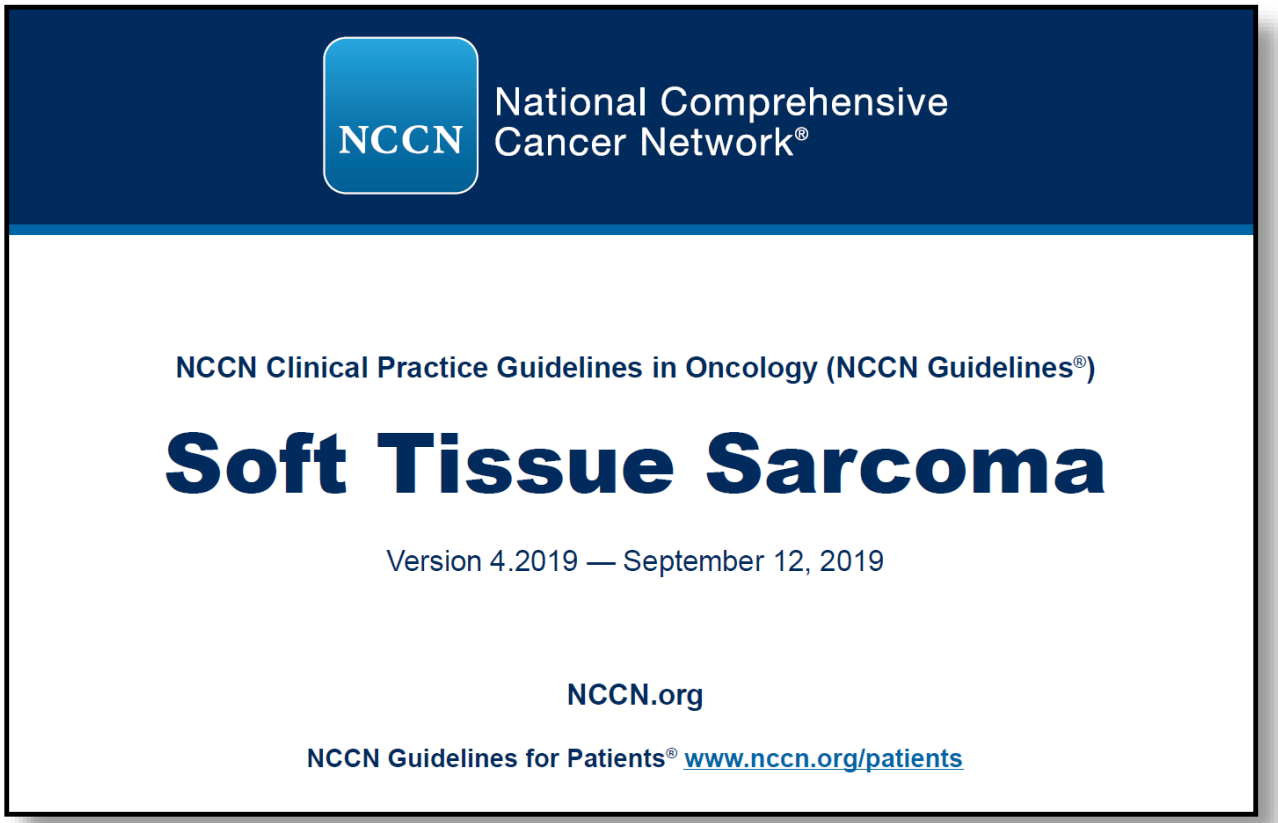
Weigh the balance between the trauma of therapy and the progression of the disease.

“Dolce far niente”

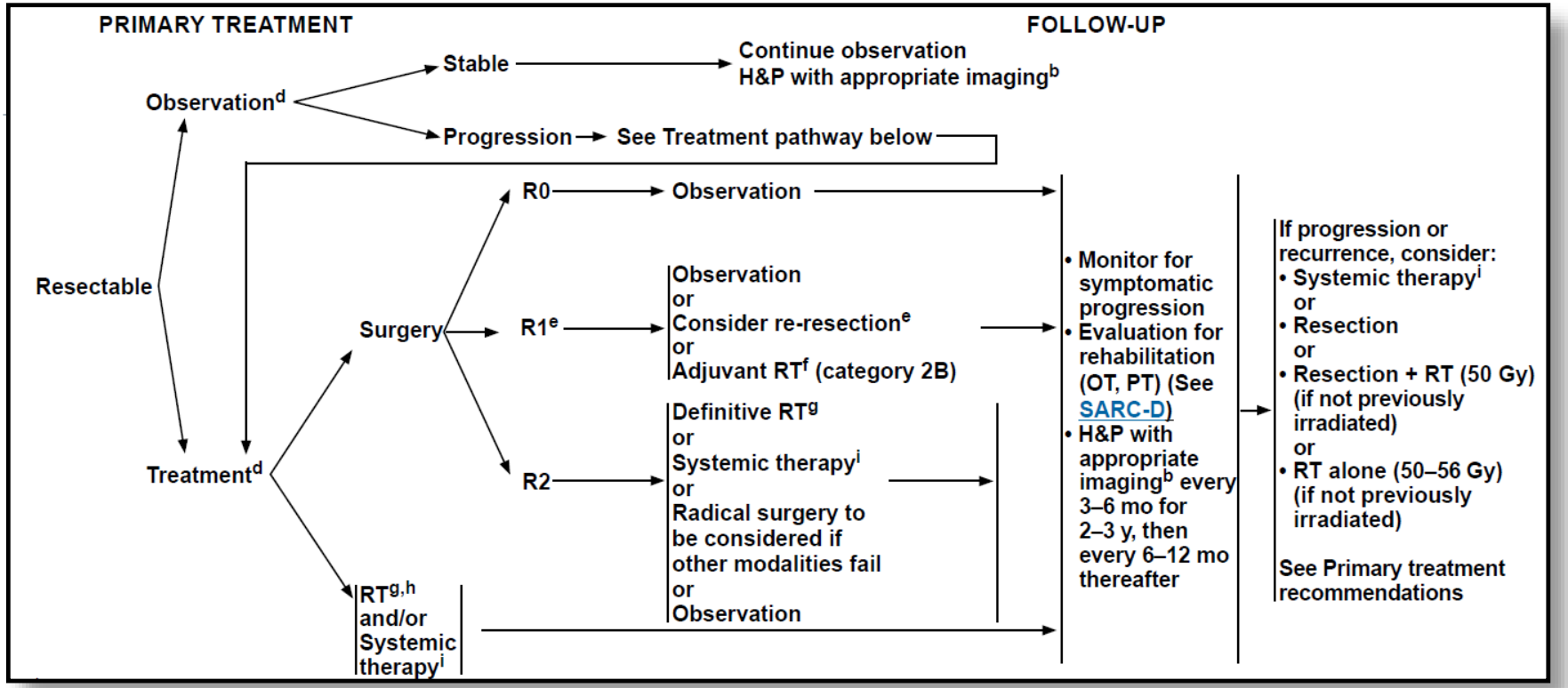
=> the sweetness of doing nothing

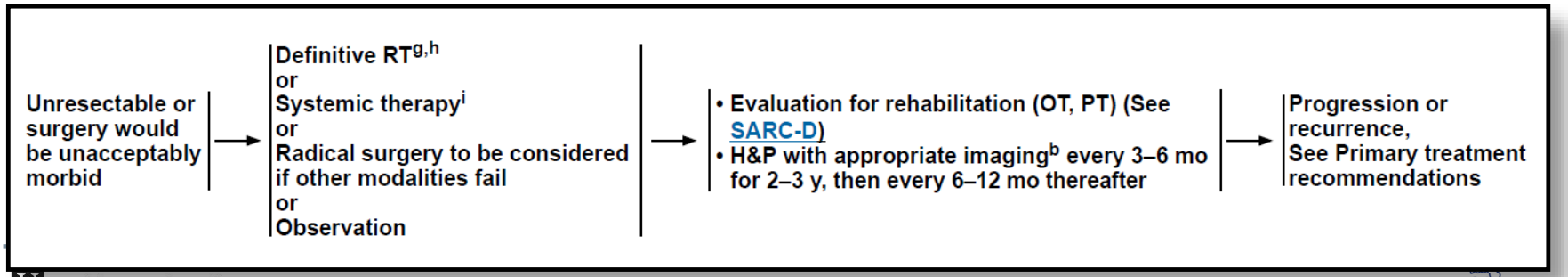


GUIDELINES

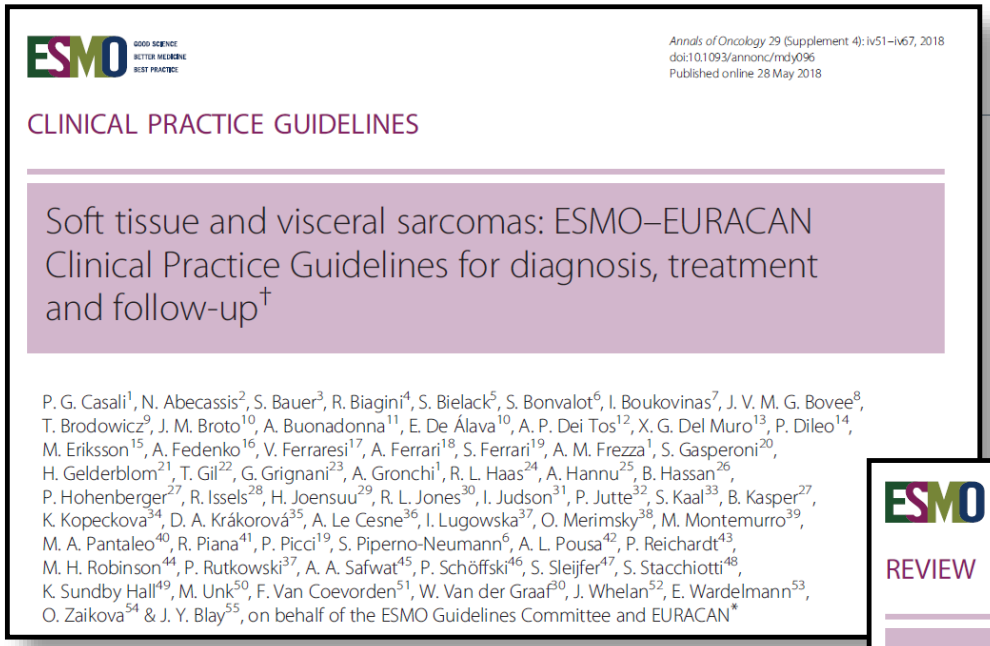

NCCN
National Comprehensive Cancer Network®
NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)
Soft Tissue Sarcoma
Version 4.2019 — September 12, 2019
NCCN.org
NCCN Guidelines for Patients® www.nccn.org/patients

GUIDELINES: NCCN





GUIDELINES

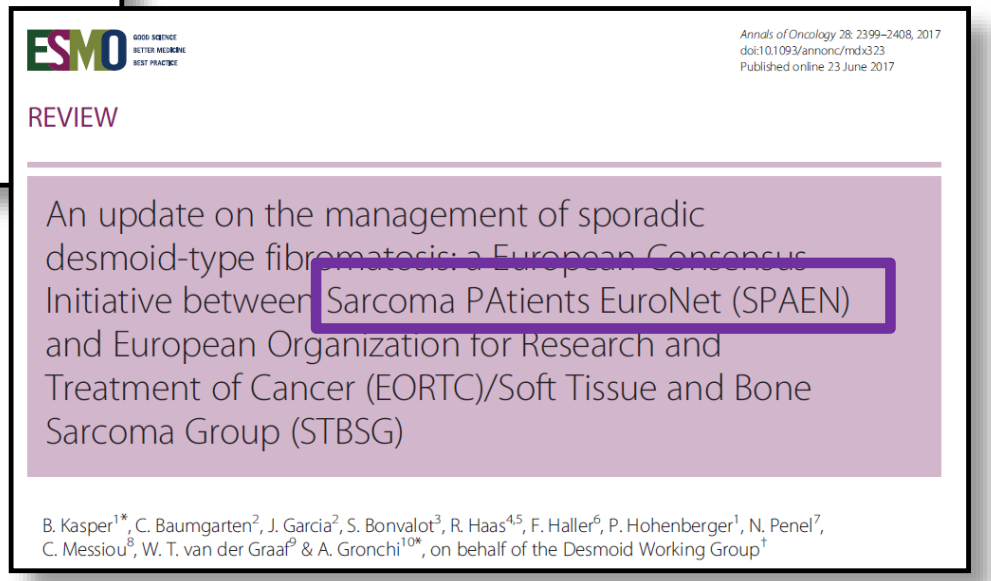


Annals of Oncology 29 (Supplement 4): iv51–iv67, 2018
doi:10.1093/annonc/mdy096
Published online 28 May 2018

CLINICAL PRACTICE GUIDELINES

Soft tissue and visceral sarcomas: ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up†

P. G. Casali[1], N. Abecassis[2], S. Bauer[3], R. Biagini[4], S. Bielack[5], S. Bonvalot[6], I. Boukovinas[7], J. V. M. G. Bovee[8], T. Brodowicz[9], J. M. Broto[10], A. Buonadonna[11], E. De Álava[10], A. P. Dei Tos[12], X. G. Del Muro[13], P. Dileo[14], M. Eriksson[15], A. Fedenko[16], V. Ferraresi[17], A. Ferrari[18], S. Ferrari[19], A. M. Frezza[1], S. Gasperoni[20], H. Gelderblom[21], T. Gil[22], G. Grignani[23], A. Gronchi[1], R. L. Haas[24], A. Hannu[25], B. Hassan[26], P. Hohenberger[27], R. Issels[28], H. Joensuu[29], R. L. Jones[30], I. Judson[31], P. Jutte[32], S. Kaal[33], B. Kasper[27], K. Kopeckova[34], D. A. Krákorová[35], A. Le Cesne[36], I. Lugowska[37], O. Merimsky[38], M. Montemurro[39], M. A. Pantaleo[40], R. Piana[41], P. Picci[19], S. Piperno-Neumann[6], A. L. Pousa[42], P. Reichardt[43], M. H. Robinson[44], P. Rutkowski[37], A. A. Safwat[45], P. Schöffski[46], S. Sleijfer[47], S. Stacchiotti[48], K. Sundby Hall[49], M. Unk[50], F. Van Coevorden[51], W. Van der Graaf[30], J. Whelan[52], E. Wardelmann[53], O. Zaikova[54] & J. Y. Blay[55], on behalf of the ESMO Guidelines Committee and EURACAN*



Annals of Oncology 28: 2399–2408, 2017
doi:10.1093/annonc/mdx323
Published online 23 June 2017

REVIEW

An update on the management of sporadic desmoid-type fibromatosis: a European Consensus Initiative between Sarcoma PAtients EuroNet (SPAEN) and European Organization for Research and Treatment of Cancer (EORTC)/Soft Tissue and Bone Sarcoma Group (STBSG)

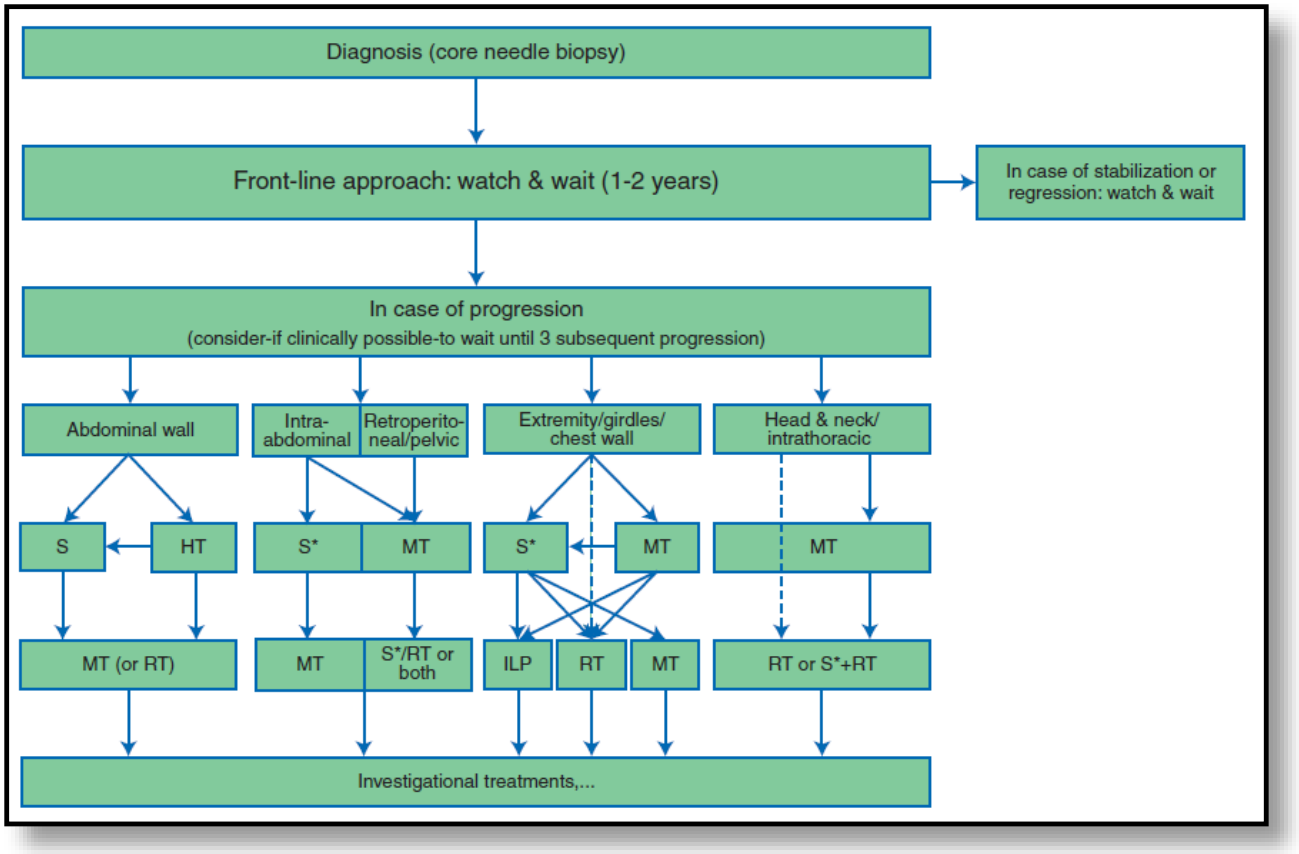
B. Kasper[1]*, C. Baumgarten[2], J. Garcia[2], S. Bonvalot[3], R. Haas[4,5], F. Haller[6], P. Hohenberger[1], N. Penel[7], C. Messiou[8], W. T. van der Graaf[9] & A. Gronchi[10]*, on behalf of the Desmoid Working Group†

GUIDELINES: ESMO

"….initial watchful waiting…."

"…. Definitive RT should be considered after multiple failed lines of treatment or for tumours in critical anatomical locations where surgery would involve prohibitive risk or functional impairment…."

GUIDELINES: ESMO & SPAEN



GUIDELINES: DESMOID TUMOR WORKING GROUP

European Journal of Cancer 127 (2020) 96–107

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Review

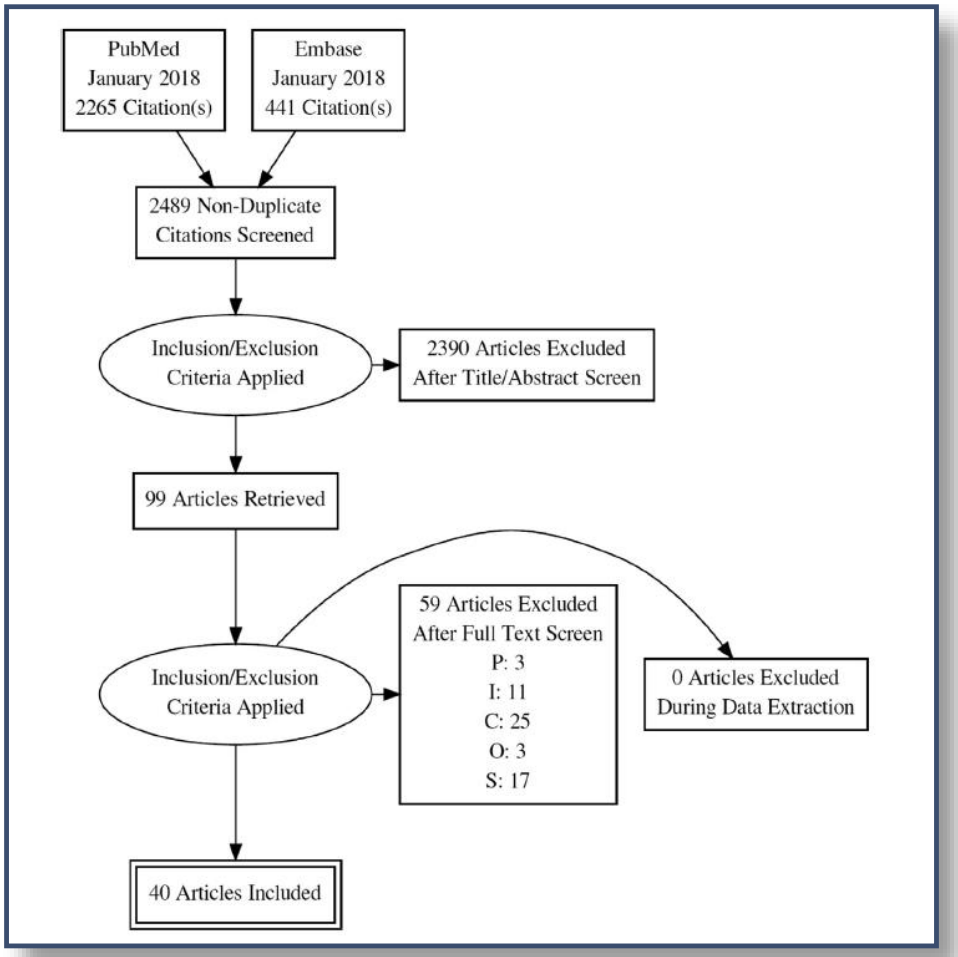
The management of desmoid tumours: A joint global consensus-based guideline approach for adult and paediatric patients

The Desmoid Tumor Working Group[1]

Led by: Dr Alessandero Gronchi (Milan) & Prof Bernd Kaspers (Mannheim)

GUIDELINES: DESMOID TUMOR WORKING GROUP

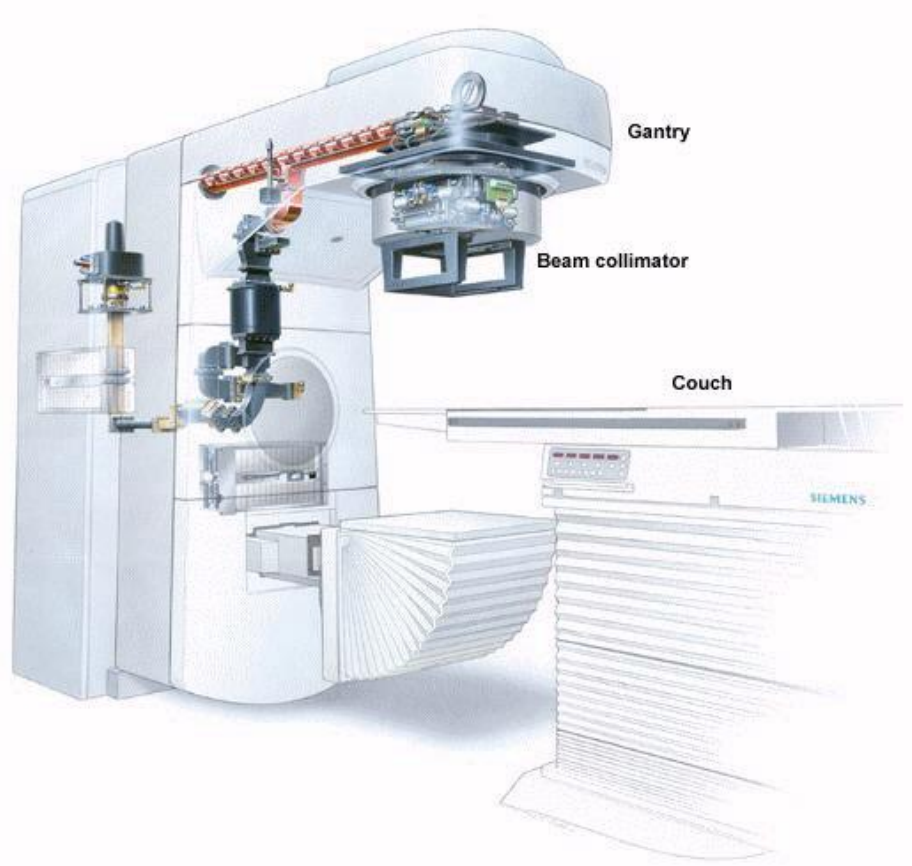
Systematic selection process for published literature



FYSICS: HOW DOES IT WORK

Linear Accelerator

= treatment machine



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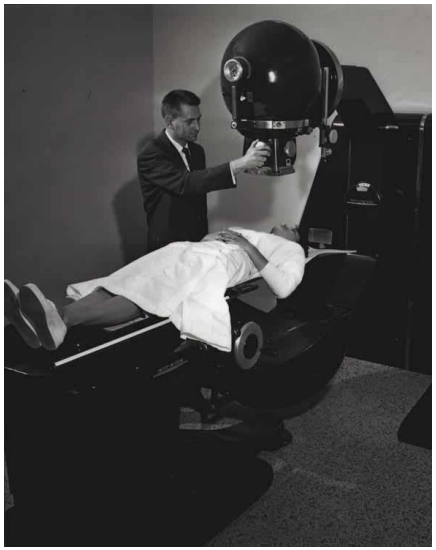
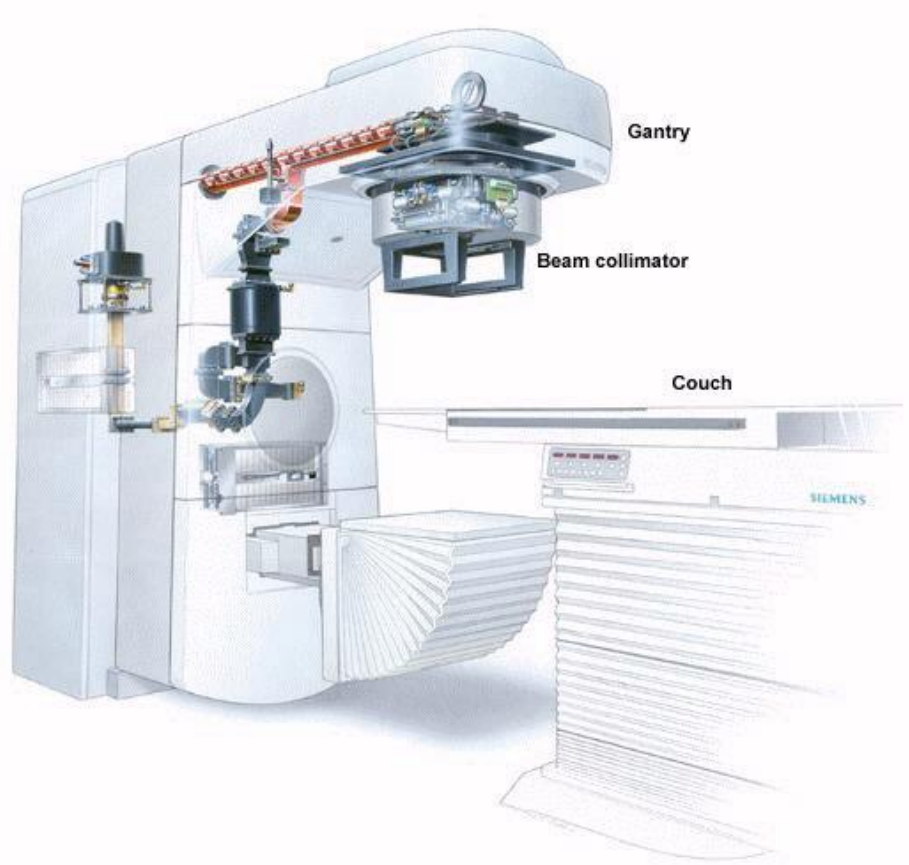
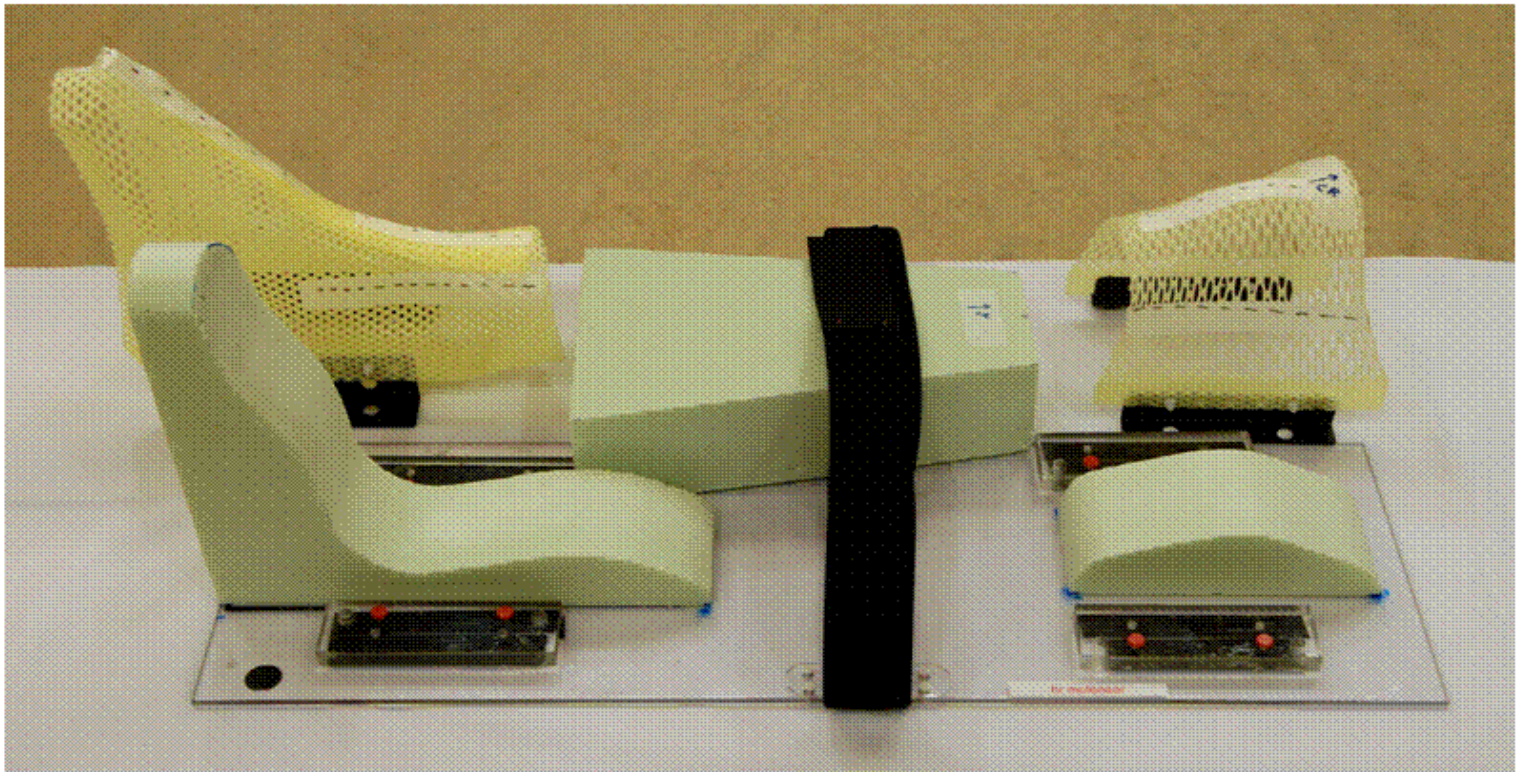
Cobalt source





FYSICS: HOW DOES IT WORK

Patient immobilization



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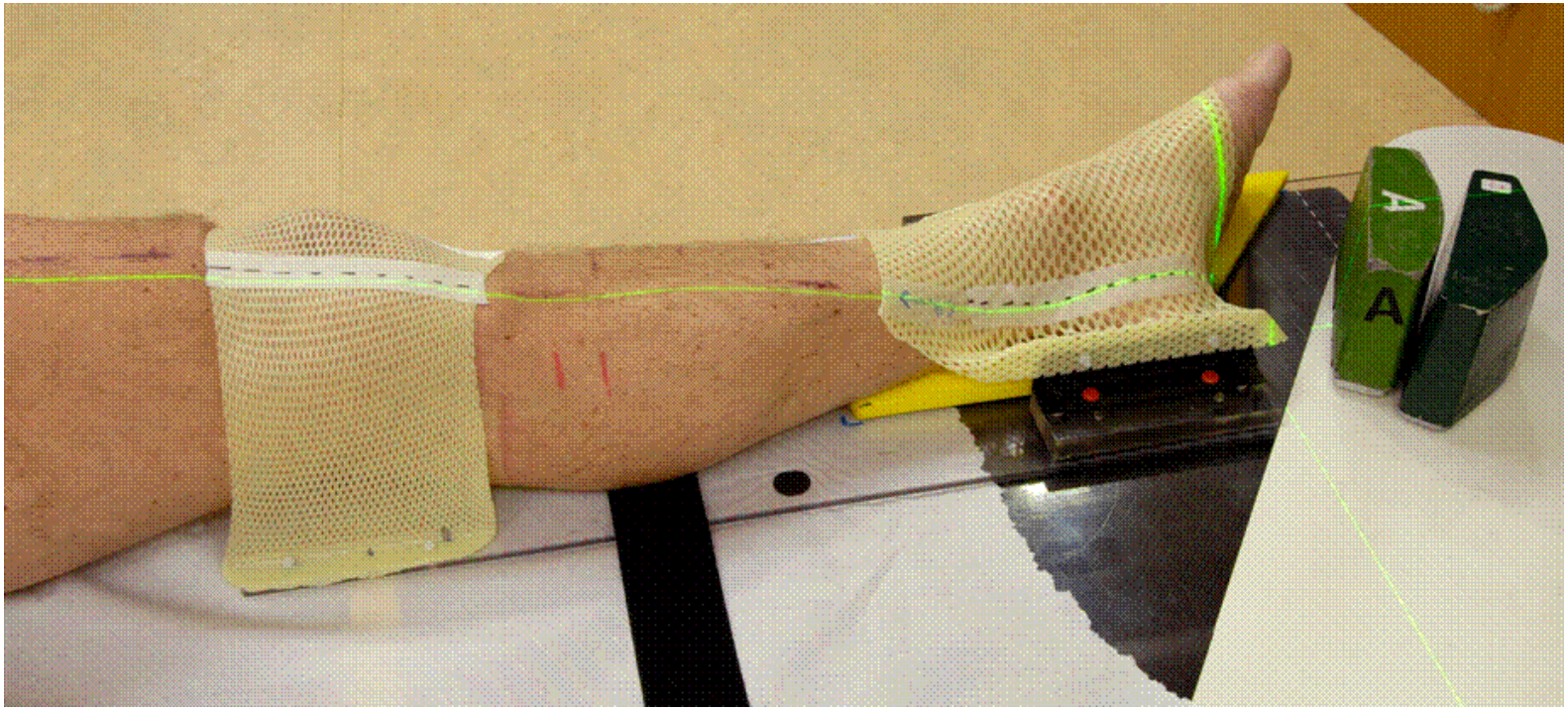
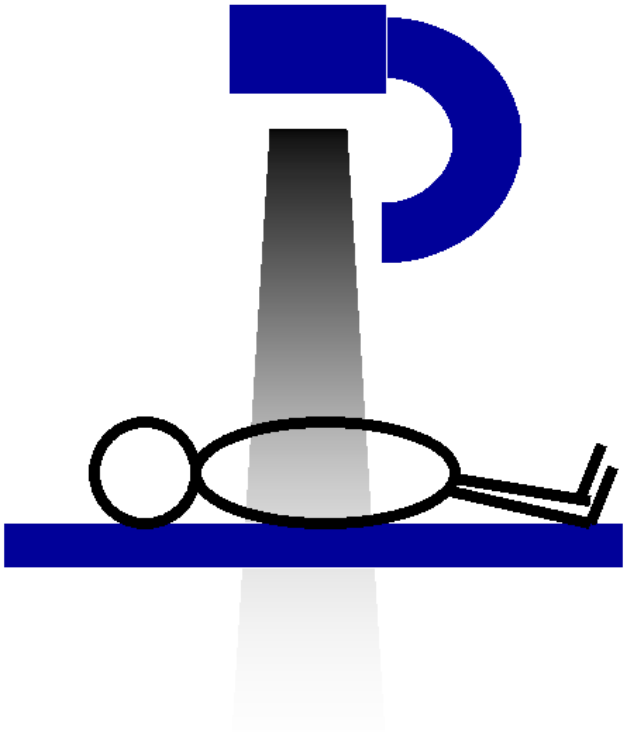


FYSICS: HOW DOES IT WORK

The further away from the head of the Linac, the less dose remains



FYSICS: HOW DOES IT WORK

Dose distribution

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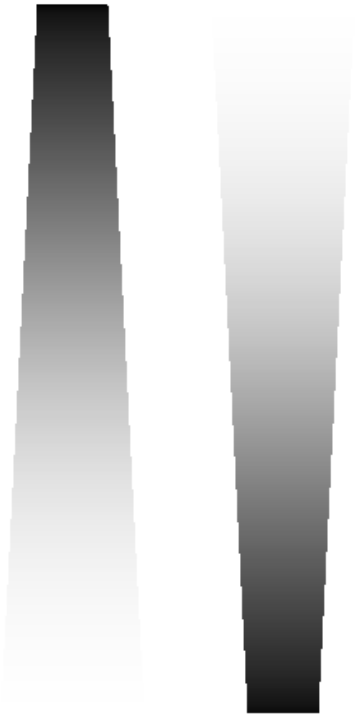
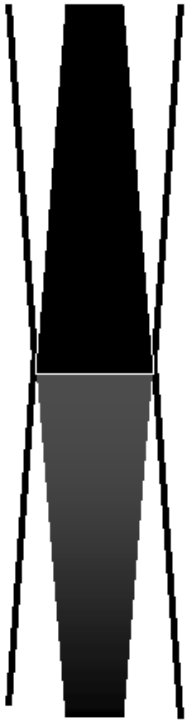
Dose distribution



FYSICS: HOW DOES IT WORK

Make use of multiple beams



a homogeneous dose distribution

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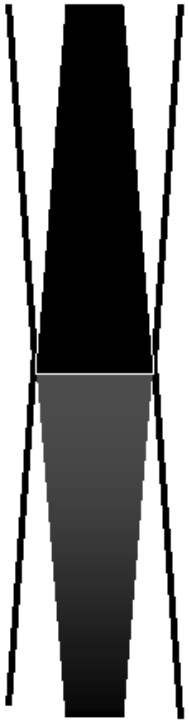
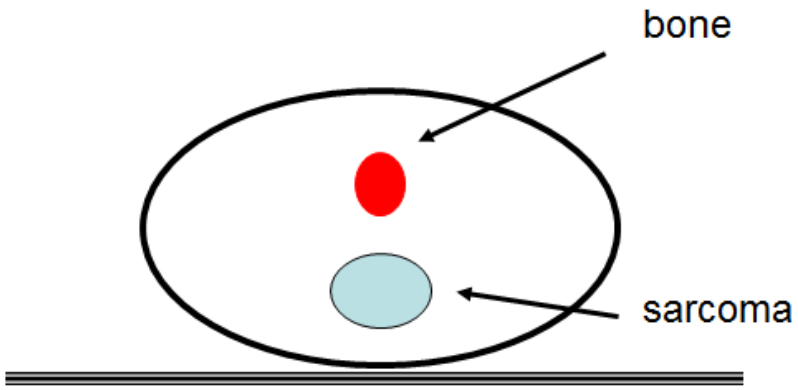
Make use of multiple beams



a homogeneous dose distribution

but…..



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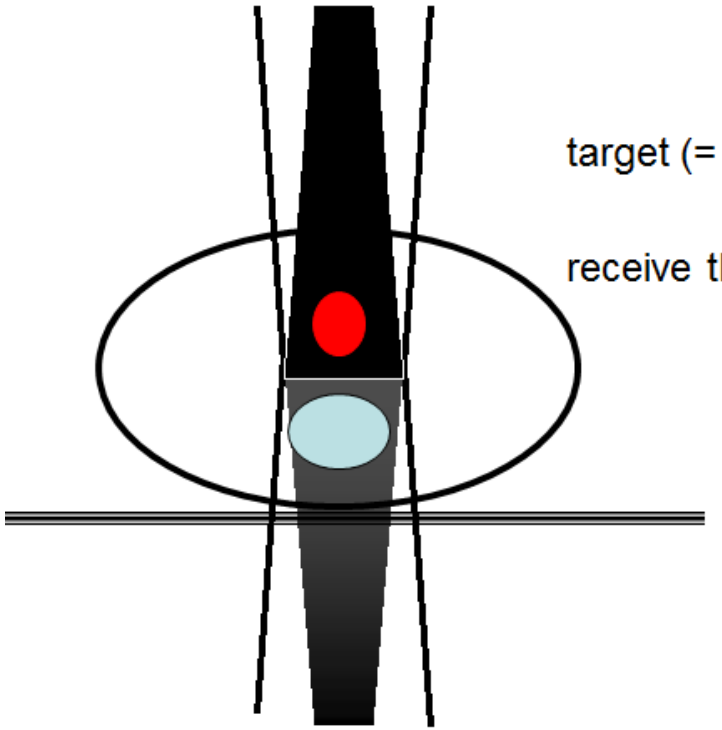
Make use of multiple beams



target (= sarcoma) and critical organ (bone)

receive the same dose **unintended**

FYSICS: HOW DOES IT WORK

Multiple beam arrangements

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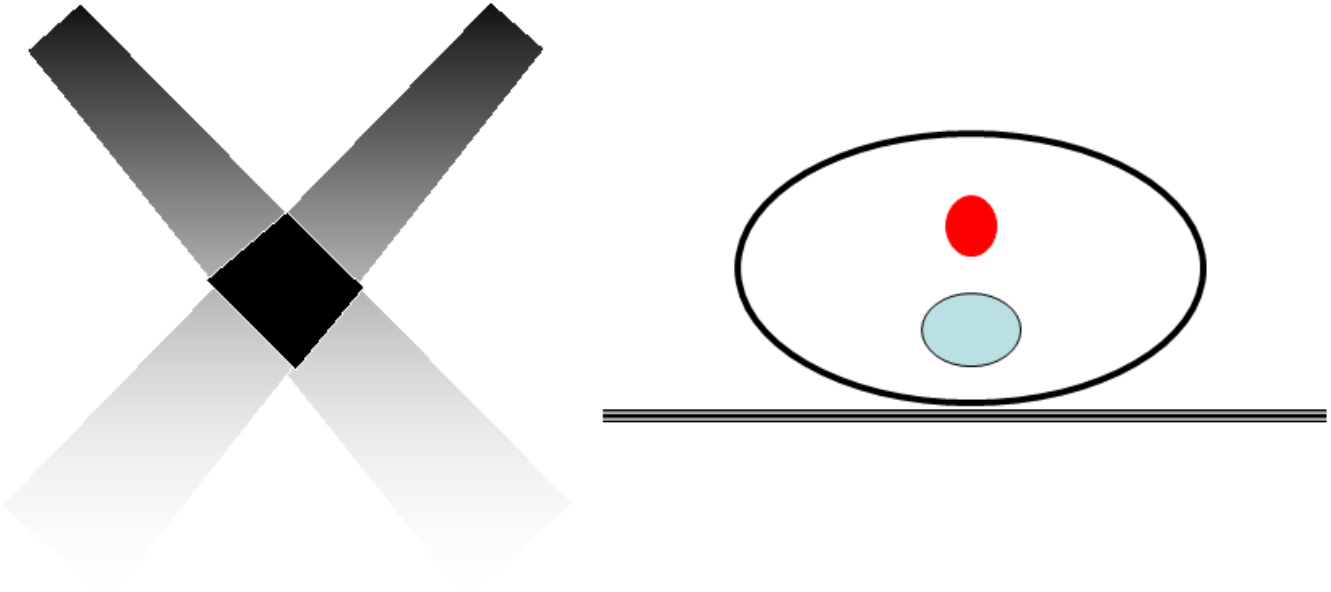
Multiple beam arrangements



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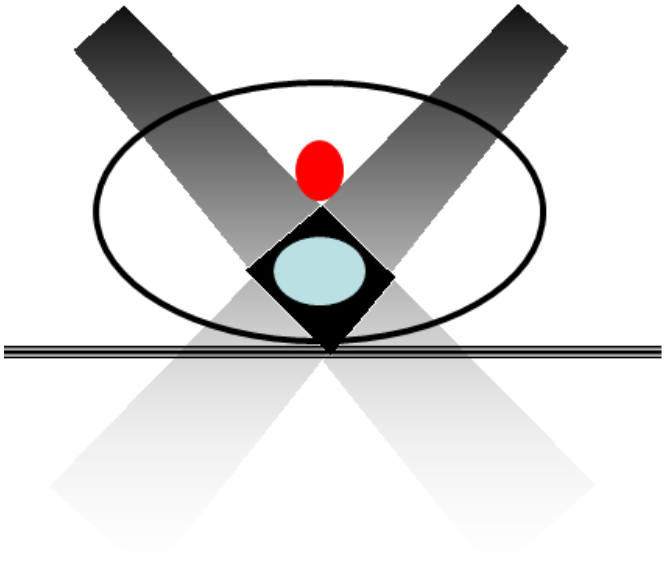
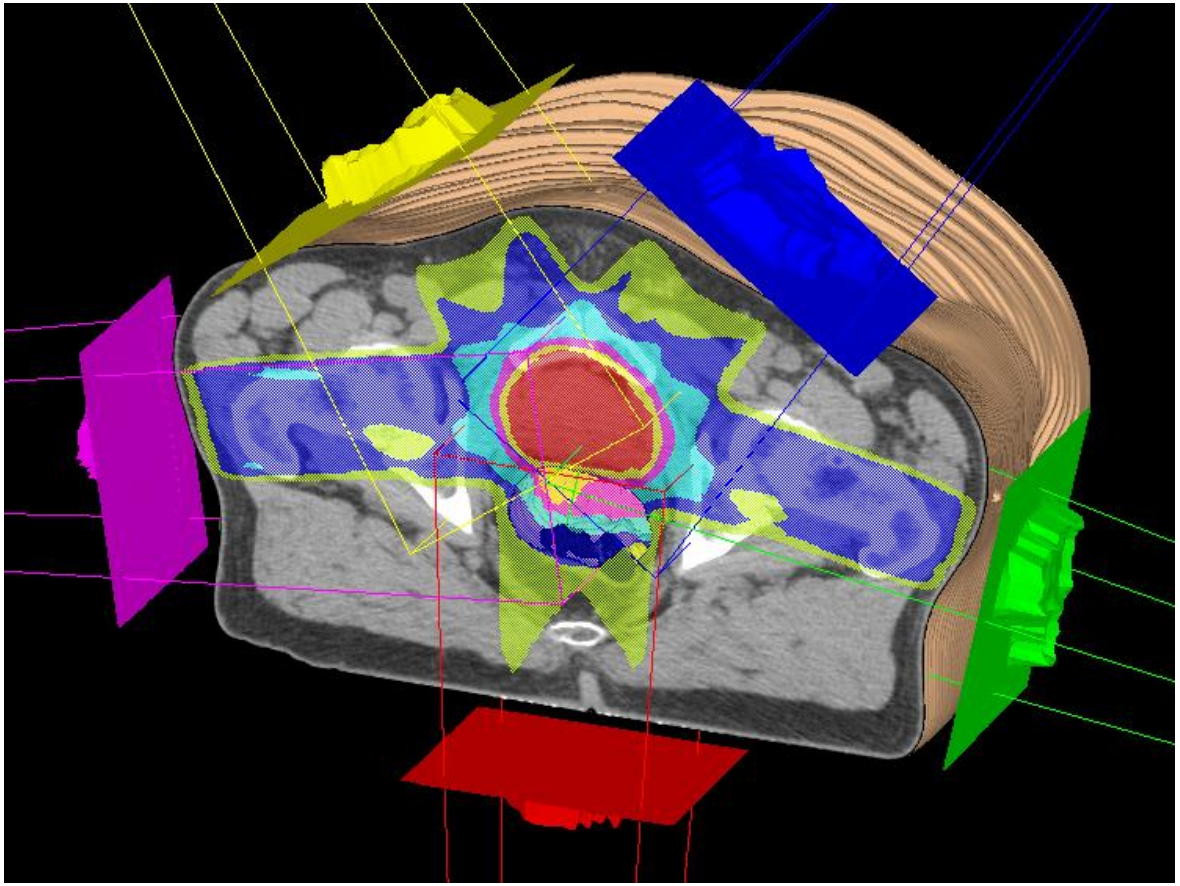


the bone receives “no” dose

whereas the sarcoma gets it all

FYSICS: INTENSITY MODULATED RT (IMRT)



IN GENERAL

decision making:
always together

(NEO-) ADJUVANT RT

The more recurrences a patient has suffered, the stronger the indication for (neo-) adjuvant RT.

NCCN guideline: consider RT in
- large tumors
- R1 resection

Note: this will be a decision for a relatively young patient with a benign disease.

RECENT LITERATURE

2017; University of Florida (n=101)

International Journal of Radiation Oncology biology • physics

www.redjournal.org

Clinical Investigation

Radiation Therapy for Aggressive Fibromatosis: The Association Between Local Control and Age

James E. Bates, MD,* Christopher G. Morris, MS,*
Nicole M. Iovino, BS,* Michael Rutenberg, MD, PhD,†
Robert A. Zlotecki, MD, PhD,* C. Parker Gibbs, MD,‡
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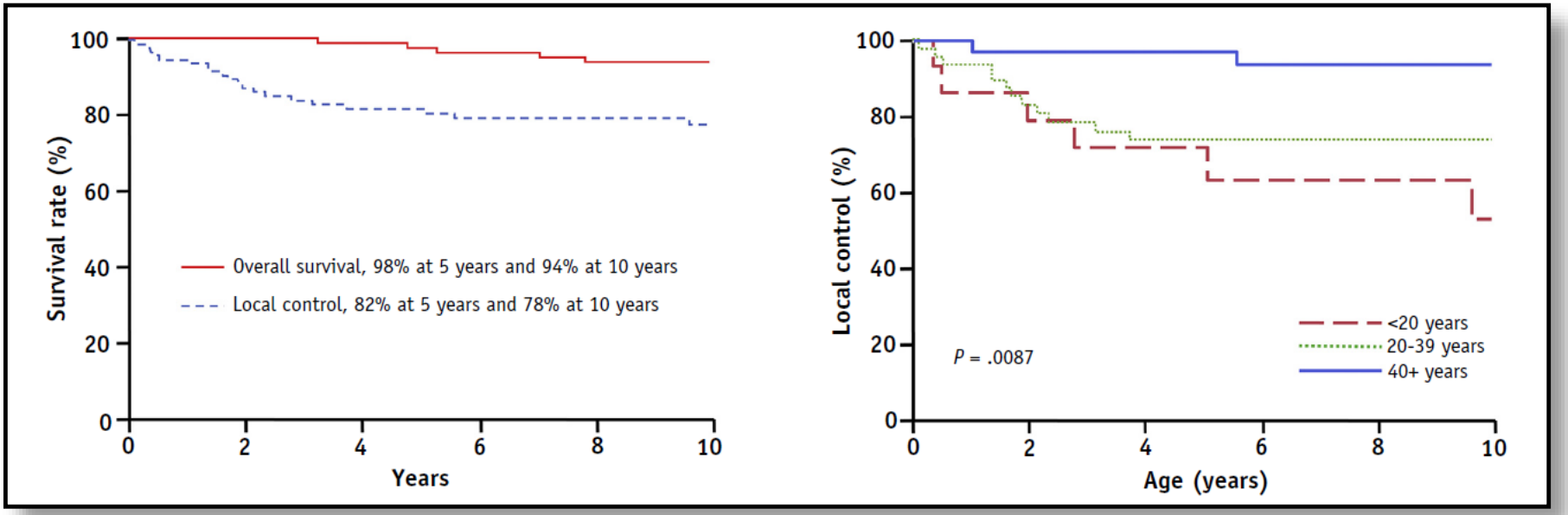
Local control 82% at 5 years
78% at 10 years

Patients < 20 years do worse: LC at 5 years 72% vs 97% (if >40 years)



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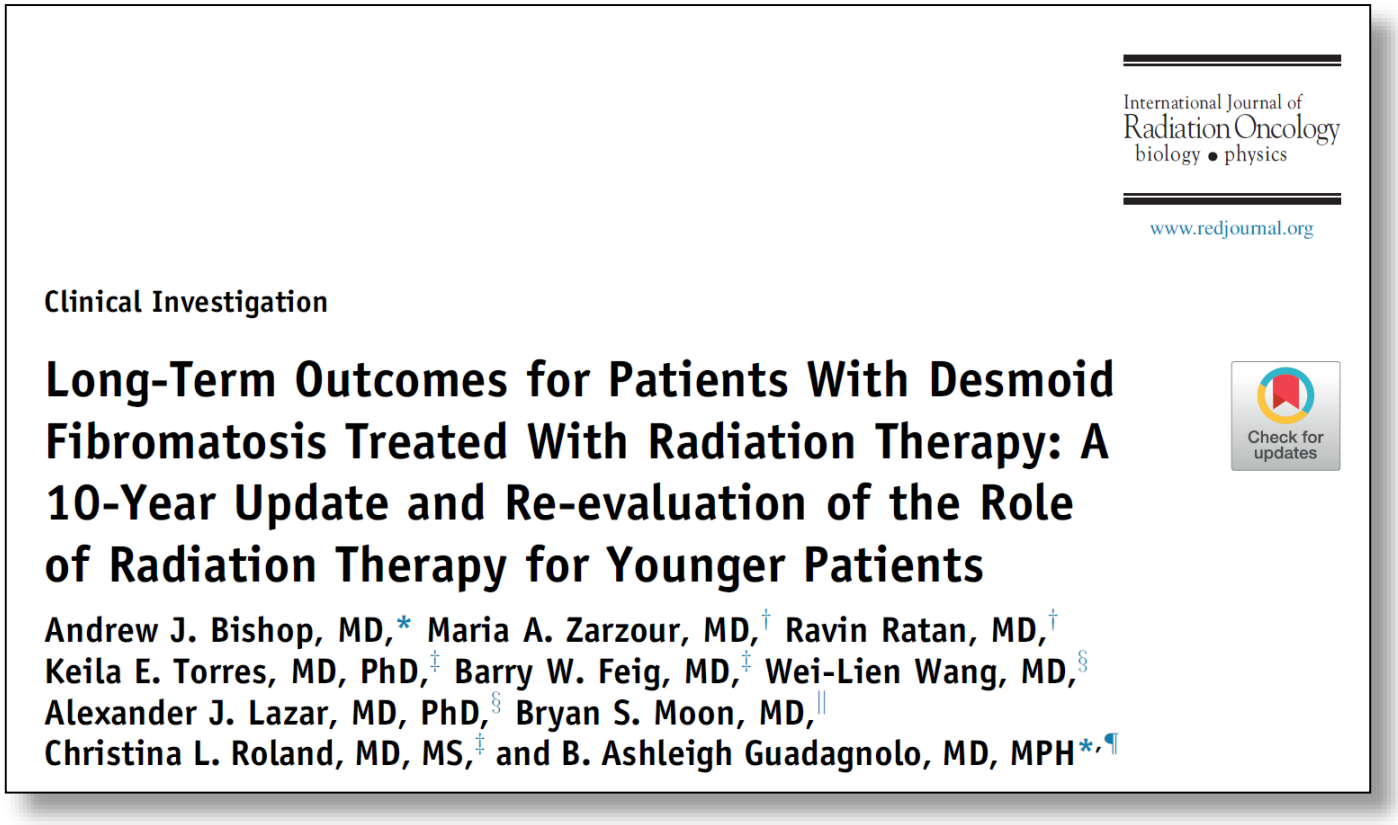
Conclusions: RT for aggressive fibromatosis offers excellent local control and should remain the standard of care for patients with unresectable or recurrent disease. Younger patients have diminished local control relative to older patients, suggesting possible biological differences contributing to radioresistance in the pediatric and young adult population.

RECENT LITERATURE

2019; MDACC 10 years FU (n=209)



International Journal of Radiation Oncology biology • physics

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Clinical Investigation

Long-Term Outcomes for Patients With Desmoid Fibromatosis Treated With Radiation Therapy: A 10-Year Update and Re-evaluation of the Role of Radiation Therapy for Younger Patients

Andrew J. Bishop, MD,* Maria A. Zarzour, MD,† Ravin Ratan, MD,†
Keila E. Torres, MD, PhD,‡ Barry W. Feig, MD,‡ Wei-Lien Wang, MD,§
Alexander J. Lazar, MD, PhD,§ Bryan S. Moon, MD,‖
Christina L. Roland, MD, MS,‡ and B. Ashleigh Guadagnolo, MD, MPH*,¶

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Local control	71% at 5 years 69% at 10 years	

For those patients with a LR (n=59, 28%), the median time to LR was 23 months

Only age (<30 years) and size (>10cm) were correlated to poor LC

Example:	LC at 5 years (if <30 years)	43%
	LC at 5 years (if >30 years)	75%

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Only age (<30 years) and size (>10cm) were correlated to poor LC

Example: LC at 5 years (if <30 years) 43%
LC at 5 years (if >30 years) 75%

Conclusions: Among all patients with desmoid fibromatosis, RT is an effective local therapy for tumor control. However, young patients ≤ 30 years have notably high rates of local recurrence regardless of treatment strategy, which requires further study. Treatment decisions should be risk-adapted by large referral centers with multidisciplinary expertise in desmoid management.

RECENT LITERATURE


Clinical Investigation

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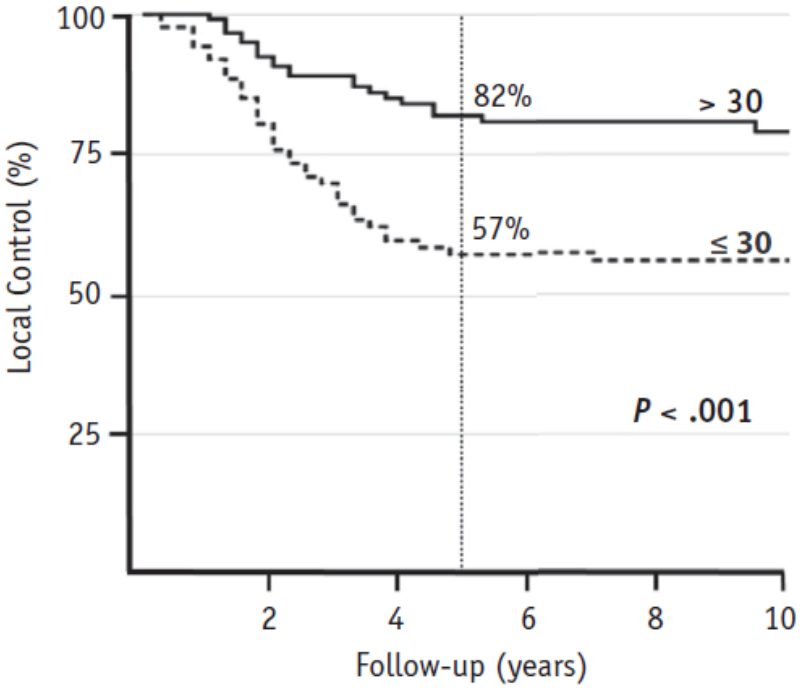

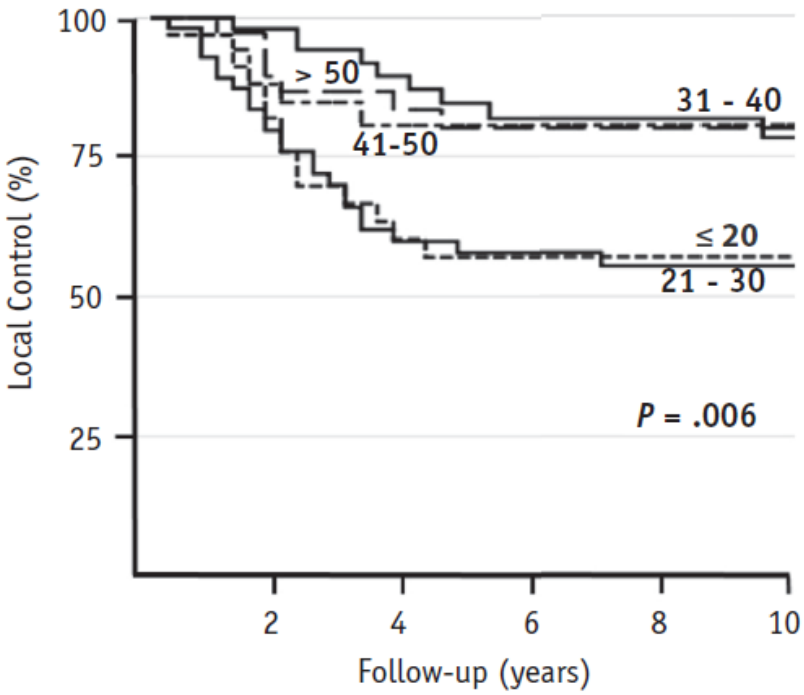

NOTES OF CAUTION

No matter how you appraise desmoids, it is not a malignant disease

Most patients are young and have a very long life expectancy

Be aware of the long term adverse effects of radiation

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Radiation may induce a second malignancy

Derived from breast cancer observations

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Most are young and have a very long life expectancy

Be aware of the long term adverse effects of radiation

Radiation may induce a second malignancy

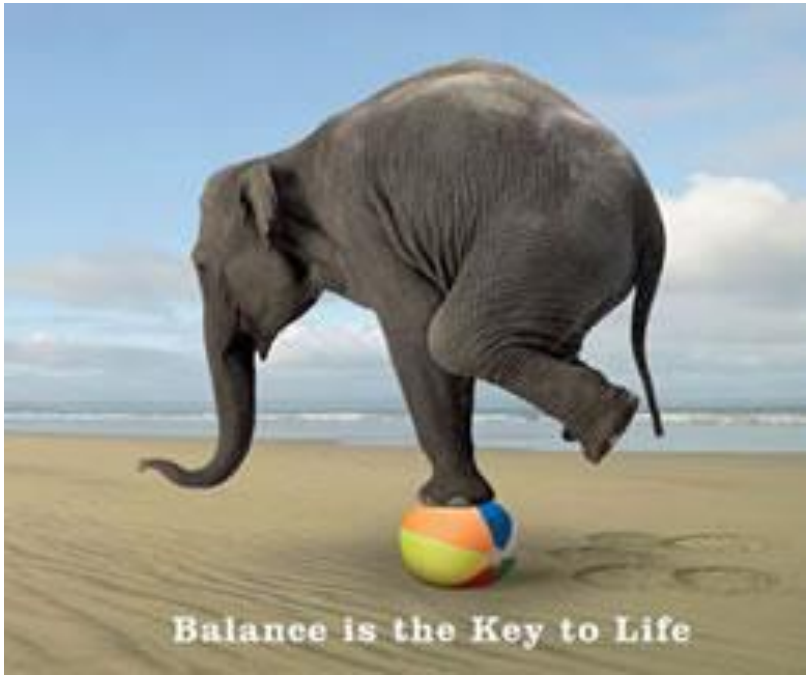
Derived from breast cancer observations

Life time risk on a radiation associated second malignancy: 0.1-0.3%

But the average age of breast cancer patients may be some 20 years older than desmoid patients

SHARED DECISION MAKING

WELL BALANCED DECISION



Sarcoma Patients EuroNet

Radiotherapy for desmoids

Rick Haas,
Dept. of Radiotherapy
the Netherlands Cancer Institute – Amsterdam
the Leiden University Medical Center

EURACAN
European network for Rare adult solid Cancer

LUMC Leiden University Medical Center

NETHERLANDS CANCER INSTITUTE
ANTONI VAN LEEUWENHOEK