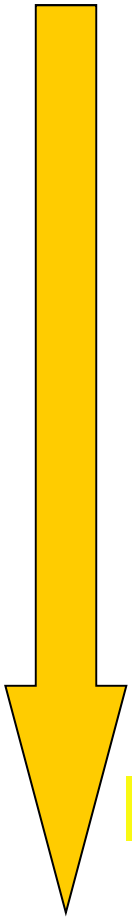
Desmoid
Wait and see

Sylvie BONVALOT

institutCurie

INDICATIONS OF AGGRESSIVE AND "DEFINITIVE" TREATMENTS (SURGERY AND RADIOTHERAPY) CHANGED OVER TIME

2005



1. Surgery when feasible
2. Wait and see for recurrent but stable lesion
3. Wait and see for primary irresectable lesion
4. The effect of surgical margins is unclear conservative approach is preferable
5. Increased use of « neo adjuvant » treatments
6. Wait and see for selected primary resectable lesions
7. Surgery is no more « standard treatment »

Bonvalot EJSO 2008, Fiore ASO 2009, Salas JCO 2012, ESMO Guidelines 2014, EORTC consensus

2015

Available online at www.sciencedirect.com
ScienceDirect
EJSO
the Journal of Cancer Surgery
EJSO 34 (2008) 462–468
www.ejso.com

Extra-abdominal primary fibromatosis: Aggressive management could be avoided in a subgroup of patients☆

S. Bonvalot [a,*], H. Eldweny [a], V. Haddad [b], F. Rimareix [a], G. Missenard [a], O. Oberlin [c], D. Vanel [d], P. Terrier [e], J.Y. Blay [f], A. Le Cesne [g], C. Le Péchoux [h]

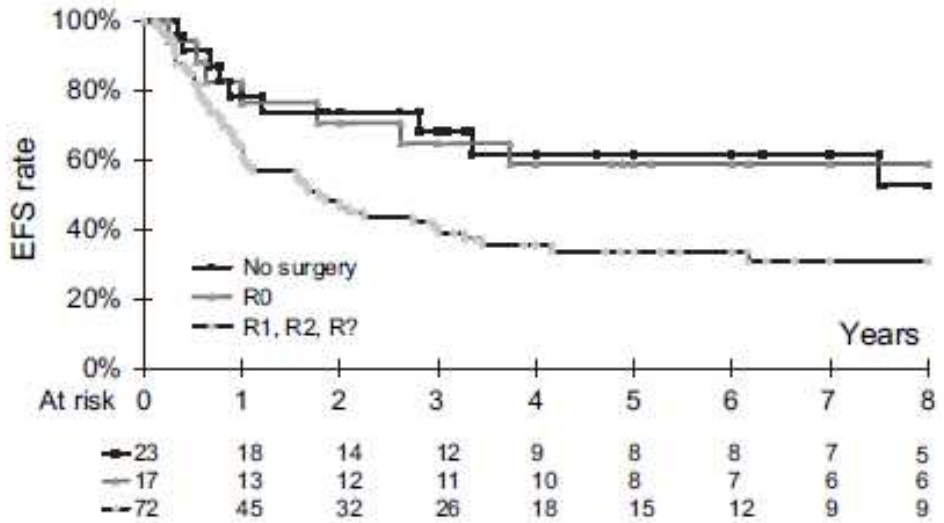


Figure 2. Event-free survival according to the quality of surgery (R0 versus no-surgery versus R1, R2, R not evaluated) (R? = R not evaluated).

Observation

- 5-year PFS: 49.9% for the W&S group (these pts were over treated before)
- 5-year PFS: 58.6% for the medical therapy group
- 50 % pts with primary avoid any treatment
- For pts who progressed, median TTP: 14 months

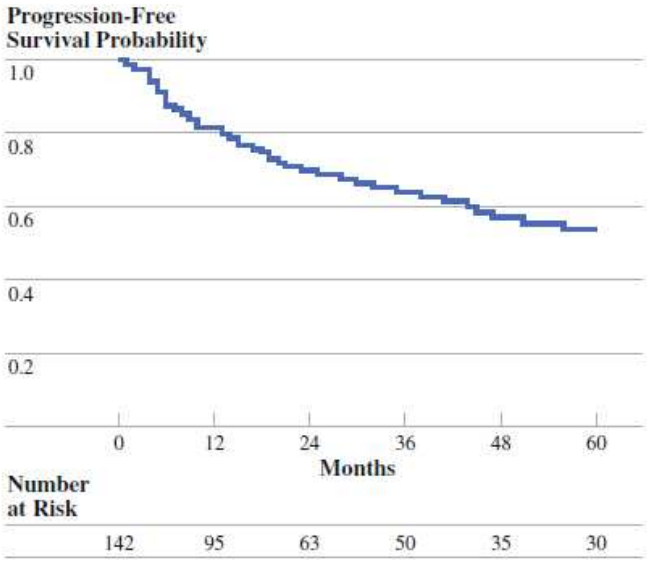


FIG. 1 Progression-free survival in the whole series

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Annals of
SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BONE AND SOFT TISSUE SARCOMAS

Desmoid-Type Fibromatosis: A Front-Line Conservative Approach to Select Patients for Surgical Treatment

Marco Fiore, MD[1], Françoise Rimareix, MD[2], Luigi Mariani, MD[3], Julien Domont, MD[4], Paola Collini, MD[5], Cecile Le Péchoux, MD[6], Paolo G. Casali, MD[7], Axel Le Cesne, MD[4], Alessandro Gronchi, MD[1], and Sylvie Bonvalot, MD, PhD[2]

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ABSTRACT

Purpose. Surgery is still the standard treatment for desmoid-type fibromatosis (DF). Recently, the Institut Gustave Roussy (IGR), Villejuif, France, reported a series of patients treated with a front-line conservative approach (no surgery and no radiotherapy). The disease remained stable in more than half of patients. This study was designed to evaluate this approach on the natural history of the disease in a larger series of patients.

Methods. A total of 142 patients presenting to the IGR or Istituto Nazionale Tumori (INT), Milan, Italy, were initially treated using a front-line deliberately conservative policy. Their progression-free survival (PFS) was observed and a multivariate analysis was performed for major clinical variables.

Results. Seventy-four patients presented with primary tumor, 68 with recurrence. Eighty-three patients received a "wait & see" policy (W&S), whereas 59 were initially offered medical therapy (MT), mainly hormonal therapy and chemotherapy. A family history of sporadic colorectal cancer was present in 8% of patients. The 5-year PFS was 49.9% for the W&S group and 58.6% for the medically treated patients ($P = 0.3196$). Similar results emerged for primary and recurrent DF. Multivariate analysis identified no clinical variables as independent predictors of PFS. In the event of progression, all patients were subsequently managed safely.

Conclusions. A conservative policy could be a safe approach to primary and recurrent DF, which could avoid unnecessary morbidity from surgery and/or radiation therapy. Half of patients had medium-term stable disease after W&S or MT. A multidisciplinary, stepwise approach should be prospectively tested in DF.

Data were presented at the Connective Tissue Oncology Society (CTOS) 14th Annual Meeting, London, UK, November 14–17, 2008.

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Desmoid-type fibromatosis (DF) is a clonal fibroblastic proliferation marked by an infiltrative growth and an inability to metastasize.[1,2] For decades, standard treatment has been complete macroscopic surgical resection. However, sizable rates of local recurrences have been reported (range 20–60% at 5 years in major retrospective studies).[3–6] Given the unpredictable outcome of the disease and the lack of metastatic potential, the aggressiveness of surgery has evolved over time. Currently, it differs from that of soft tissue sarcomas.[4–8] In fact, until 1998 the standard treatment for DF consisted of primary resection with wide margins, possibly with radiotherapy when negative margins could not be achieved or surgery would have resulted in major functional or cosmetic defects.[9] Later, function-preserving surgery was advocated for DF, with particular emphasis on limiting unnecessary morbidity.[4–6] A "wait & see" (W&S) policy alone was first proposed for recurrent but stable lesions.[10] An initial period of observation also was considered for unresectable primary tumors.[11] Furthermore, DF may respond to chemotherapy or other systemic treatments

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ORIGINAL ARTICLE – BONE AND SOFT TISSUE SARCOMAS

Spontaneous Regression of Primary Abdominal Wall Desmoid Tumors: More Common than Previously Thought

Sylvie Bonvalot, MD, PhD[1], Nils Ternès, MS[2], Marco Fiore, MD[3], Georgina Bitsakou, MD[1], Chiara Colombo, MD[3], Charles Honoré, MD[1], Andrea Marrari, MD[4], Axel Le Cesne, MD[5], Federica Perrone, MD[6], Ariane Dunant, MS[2], and Alessandro Gronchi, MD[3]

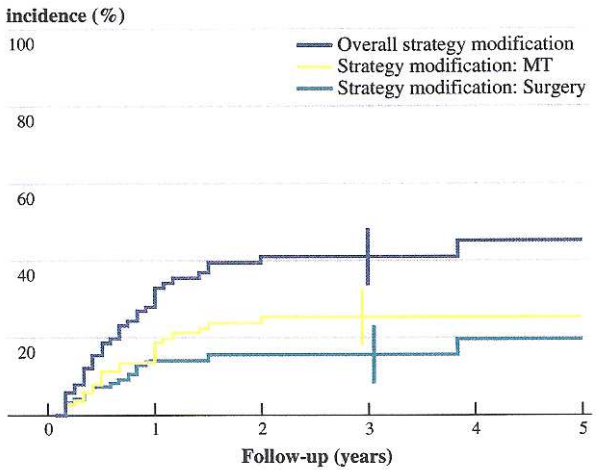

FIG. 2 Cumulative incidence of overall strategy modification, switch to medical treatment with no further switch, and final switch to surgery

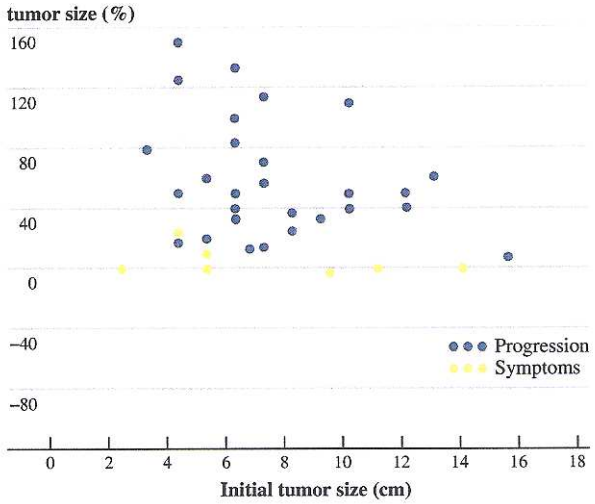

FIG. 3 Change in tumor size for patients with modification strategy (each *point* represents a patient)

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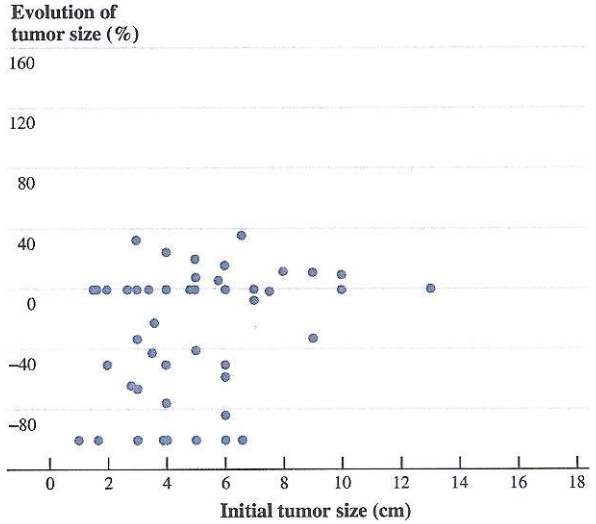

FIG. 4 Change in tumor size for patients without modification strategy (each *point* represents a patient)

147 patients

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European Journal of Cancer (2015) 51, 186–192

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Sporadic extra abdominal wall desmoid-type fibromatosis: Surgical resection can be safely limited to a minority of patients

C. Colombo [a], R. Miceli [b], C. Le Péchoux [c], E. Palassini [d], C. Honoré [e], S. Stacchiotti [d], O. Mir [f], P.G. Casali [d], J. Dômont [f], M. Fiore [a], A. Le Cesne [f], A. Gronchi [a,*], S. Bonvalot [e]

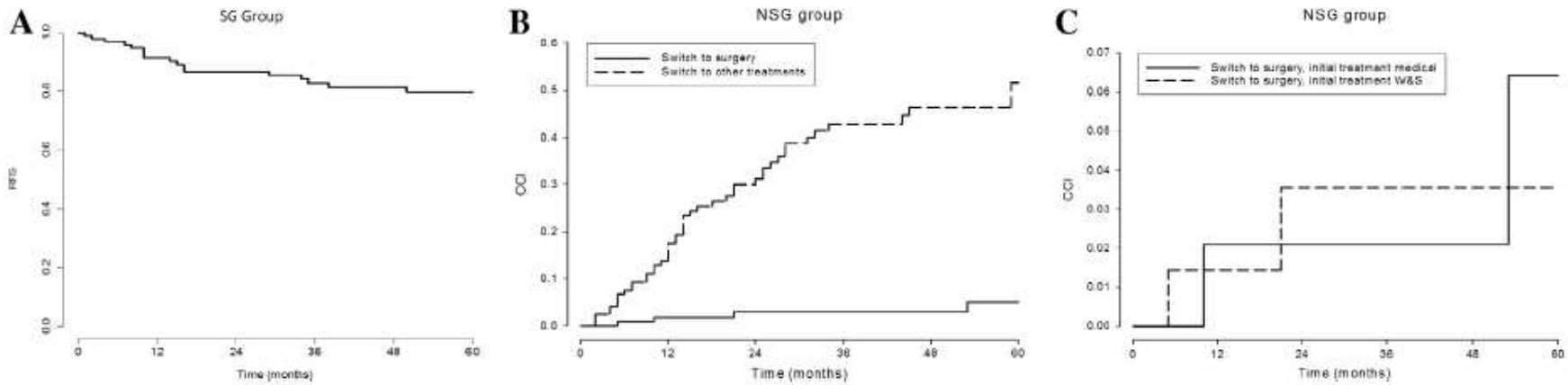

Fig. 1. Recurrence free survival for patients in surgical (SG) (panel A); crude cumulative incidence (CCI) of switch strategy in non-surgical (NSG) group: switch to surgery versus other treatments (Panel B) and switch to surgery if initial treatment was wait and see (W&S) versus medical treatments (Panel C).

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ORIGINAL ARTICLE – BONE AND SOFT TISSUE SARCOMAS

Toward Observation as First-line Management in Abdominal Desmoid Tumors

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[1]Division of General Surgery, Mount Sinai Hospital, Toronto, ON, Canada; [2]Department of Surgical Oncology, Princess Margaret Cancer Centre, Toronto, ON, Canada; [3]Department of Surgery, University of Toronto, Toronto, ON, Canada; [4]Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, ON, Canada; [5]University of Toronto, Toronto, ON, Canada; [6]Department of Medical Oncology, Mount Sinai Hospital, Toronto, ON, Canada; [7]Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada

with clinical practice at that time. Nonetheless, there did not appear to be any disadvantages to an initial W&S management strategy that was implemented in the second half of the time period included in our study. There may even be a benefit from this approach, as patients who have DT that spontaneously regresses can be identified and spared an unnecessary surgical procedure. Our series also

symposium article

Annals of Oncology 23 (Supplement 10): x158–x166, 2012
doi:10.1093/annonc/mds298

The treatment of desmoid tumors: a stepwise clinical approach

S. Bonvalot[1*], A. Desai[1], S. Coppola[1], C. Le Péchoux[2], P. Terrier[3], J. Dômont[4] & A. Le Cesne[4]

[1]*Departments of Surgery;* [2]*Radiotherapy;* [3]*Pathology;* [4]*Medical Oncology, Institut Gustave Roussy, Villejuif, France*

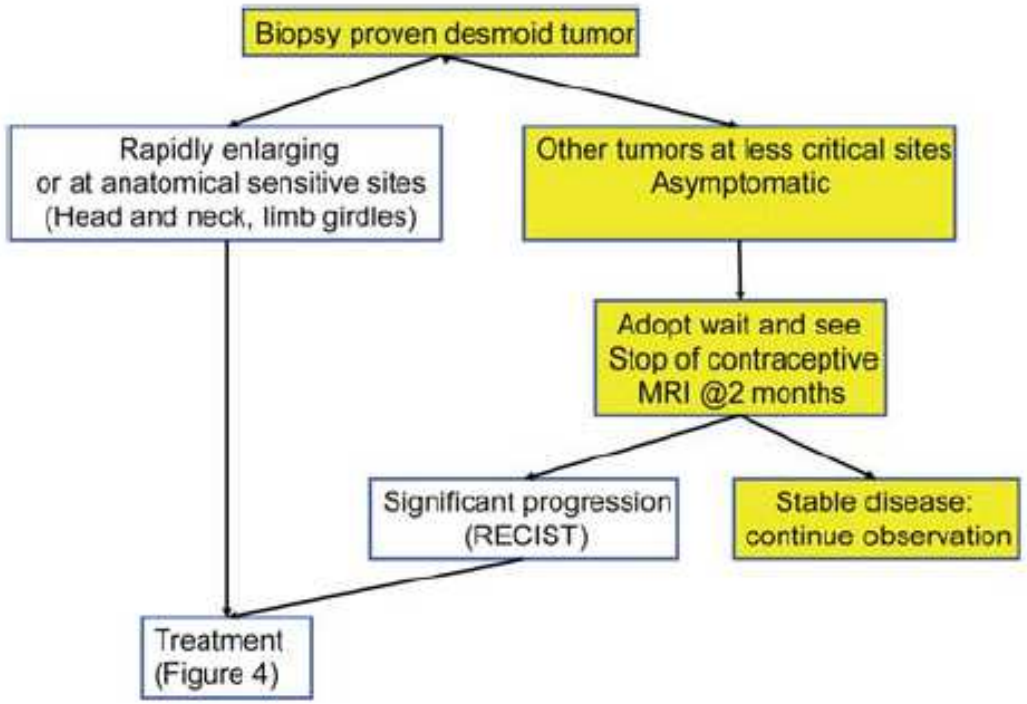

Figure 3. Initial treatment algorithm for primary desmoids.

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European Journal of Cancer (2015) 51, 127–136

Available at www.sciencedirect.com

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journal homepage: www.ejcancer.com

Position Paper

Management of sporadic desmoid-type fibromatosis: A European consensus approach based on patients' and professionals' expertise – A Sarcoma Patients EuroNet and European Organisation for Research and Treatment of Cancer/Soft Tissue and Bone Sarcoma Group initiative

B. Kasper [a,*], C. Baumgarten [b], S. Bonvalot [c], R. Haas [d], F. Haller [e], P. Hohenberger [a], G. Moreau [f], W.T.A. van der Graaf [g], A. Gronchi [h], on behalf of the Desmoid Working Group [i]

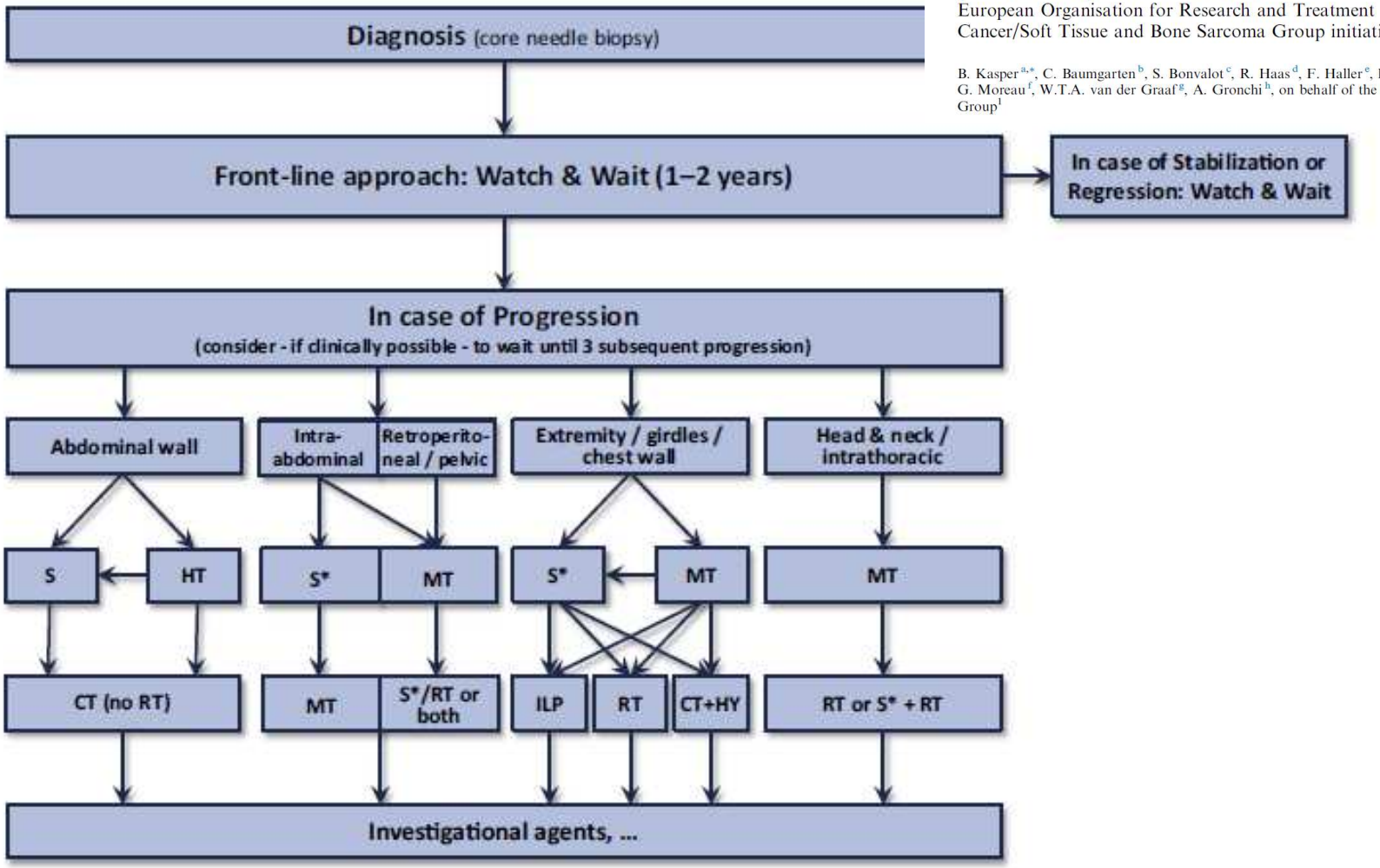
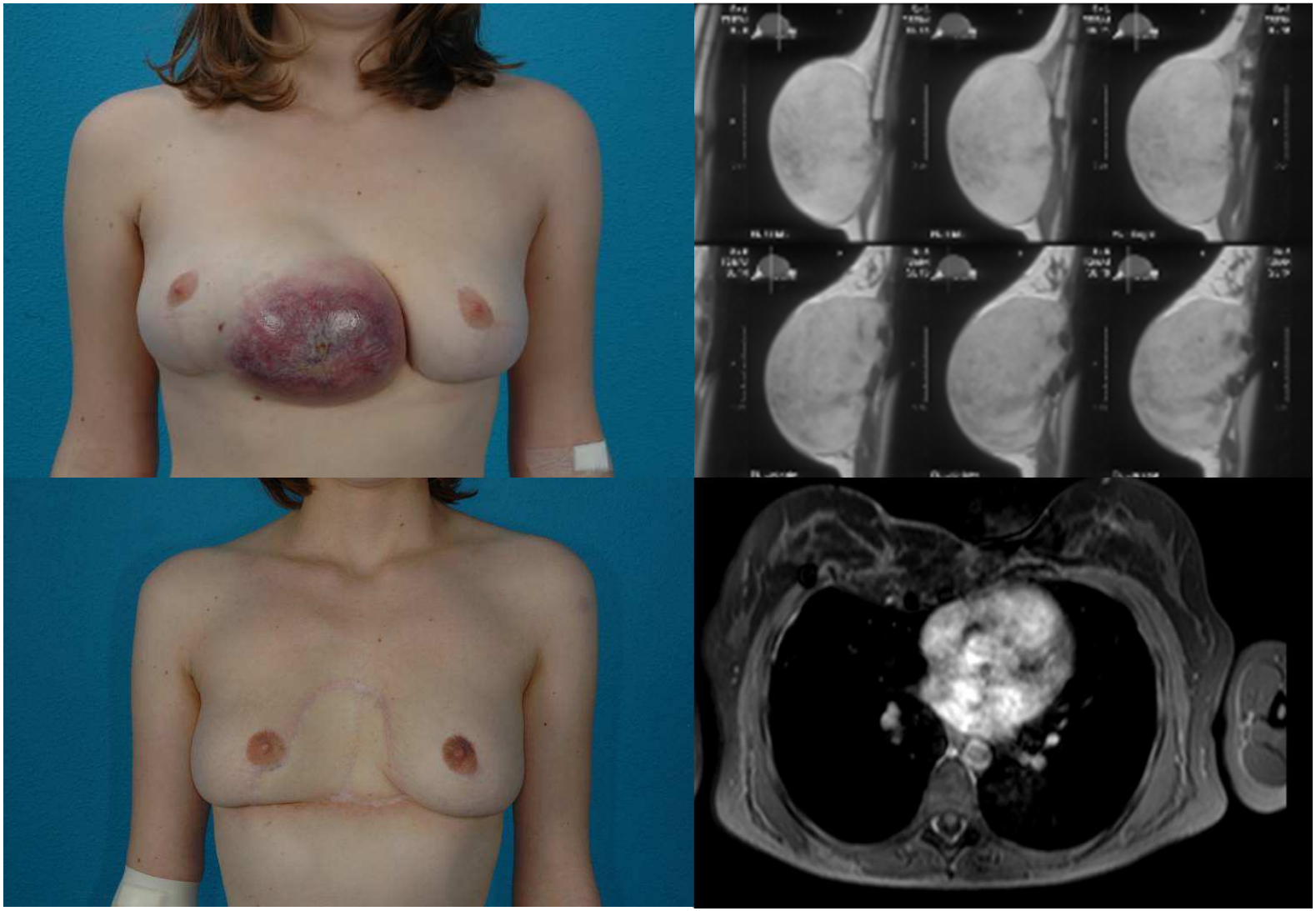


Fig. 1. Consensus algorithm. *Abbreviations:* HT, hormonal therapy; S, surgery; S*, surgery is an option if morbidity is limited; MT, medical therapy; RT, Radiotherapy; CT, chemotherapy; ILP, isolated limb perfusion; HY: hyperthermia.

Who should be operated immediately

- Complication (occlusion, perforation…)
  - Treatment of the complication without systematic resection of the tumor, specifically in PAF
- Cosmetic issue

Cosmetic issue



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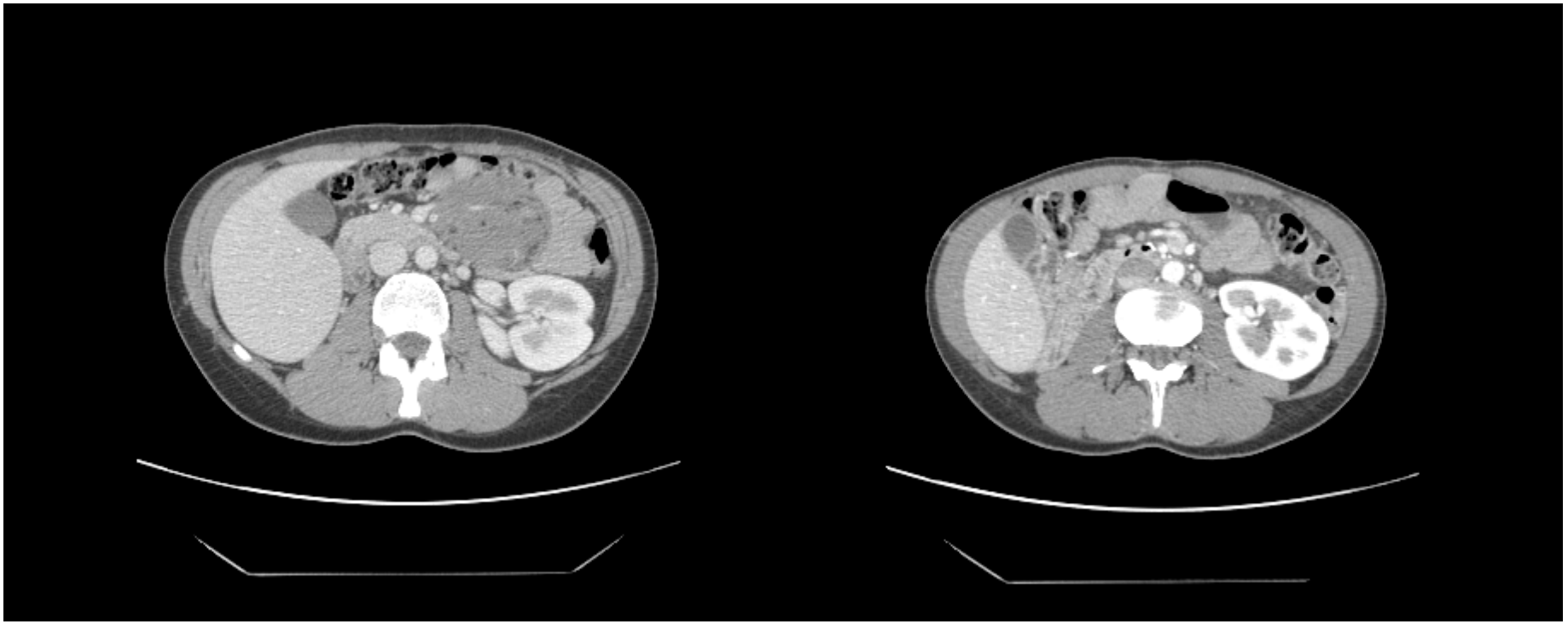
Who should be operated immediately +/-

- No diagnosis/diagnosis doubt +/-
- Size +/-
- Vital risk in case of progression and T resectable +/-

No proven diagnosis

2007

2015



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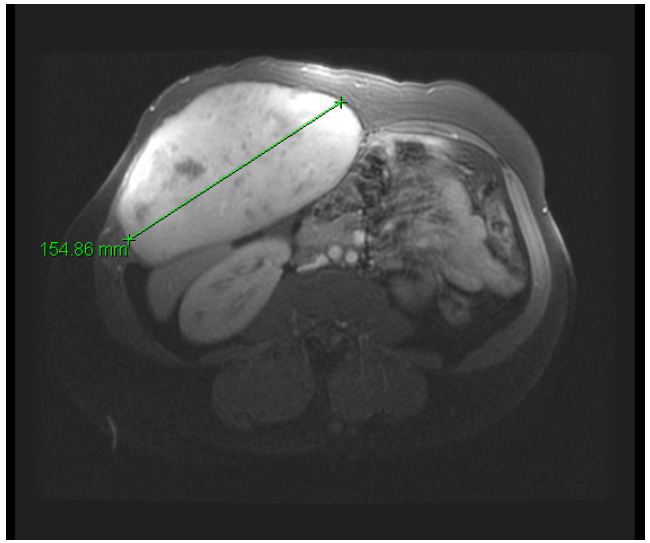
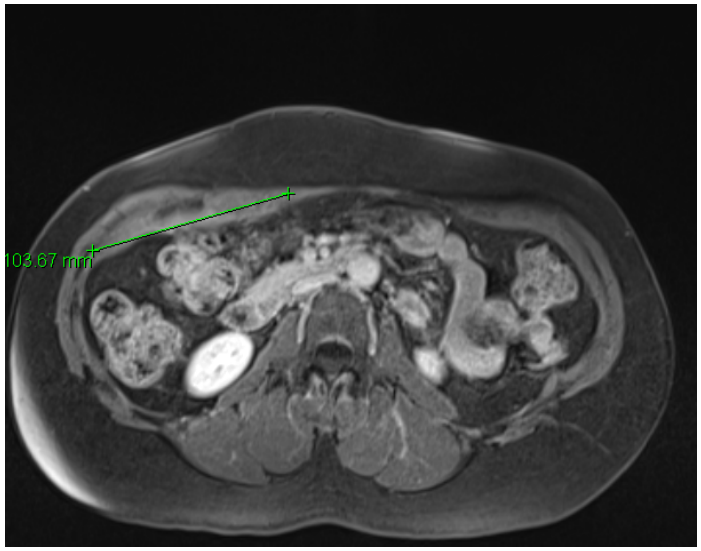
Size +/-



May 2005
Female: 50 years old
Biopsy: Desmoid (review FSG)



Oct 2011

- Size criteria is not sufficient…
- Regression/Stabilisation in desmoids is likely to have been underestimated as it has been calculated in a group of patients with recurrences where surgical options have been exhausted…

What are not sufficient reasons to operate immediately?

- Mild pain
- Patient referred for surgery
- Recurrence
- Pregnancy
- Familial adenomatous polyposis ++

  (sub/total colectomy)

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DOI 10.1245/s10434-009-0586-2

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Desmoid-Type Fibromatosis: A Front-Line Conservative Approach to Select Patients for Surgical Treatment

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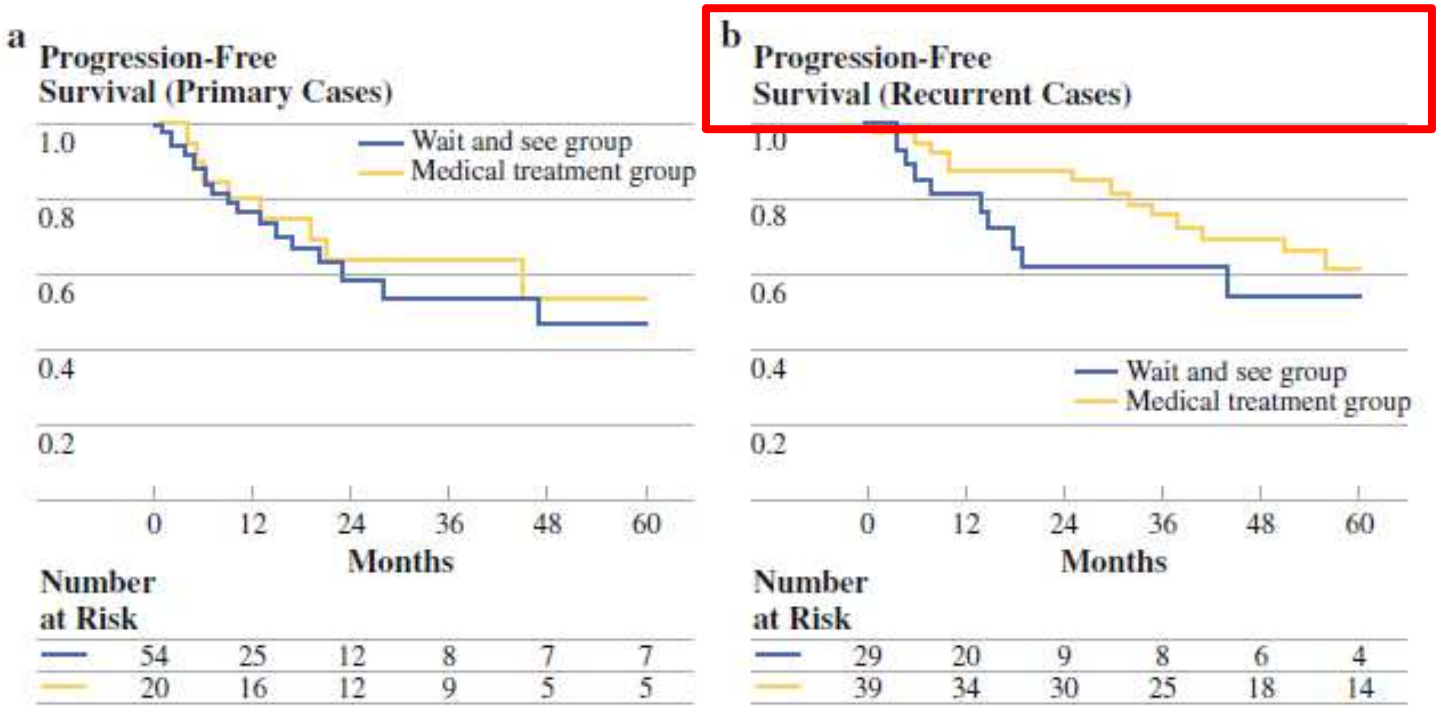
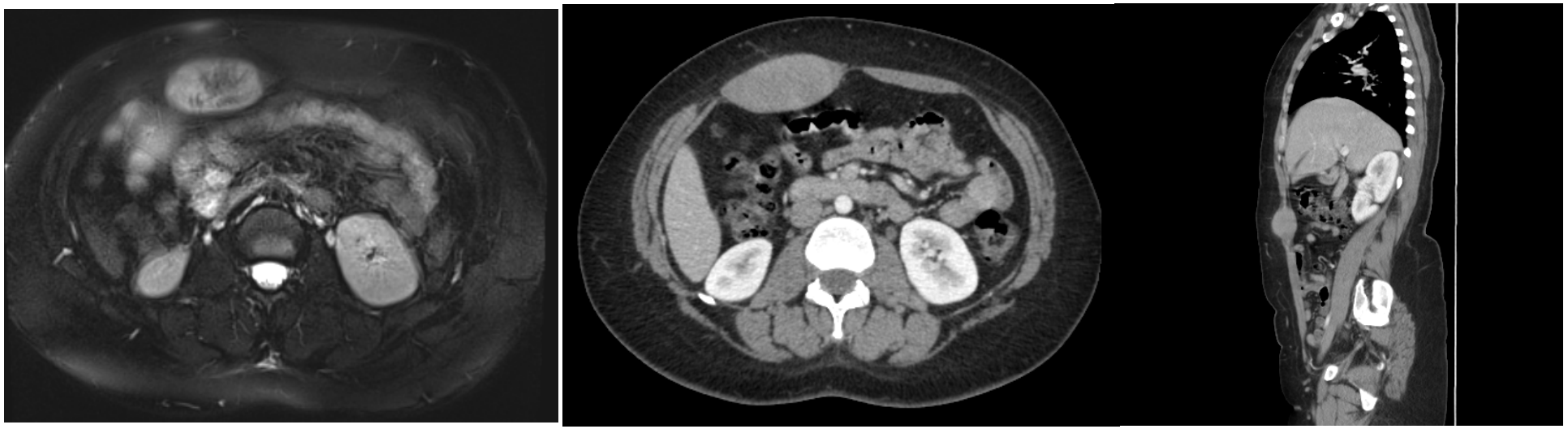
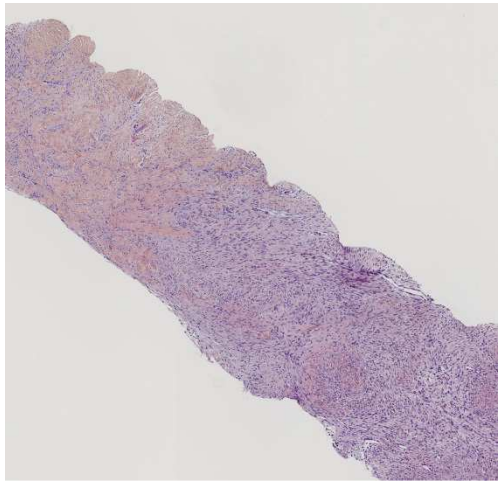
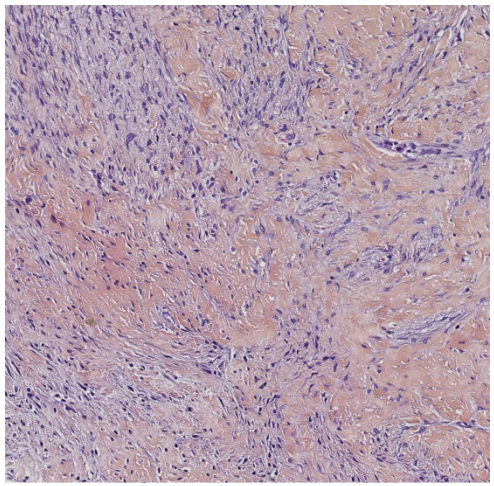


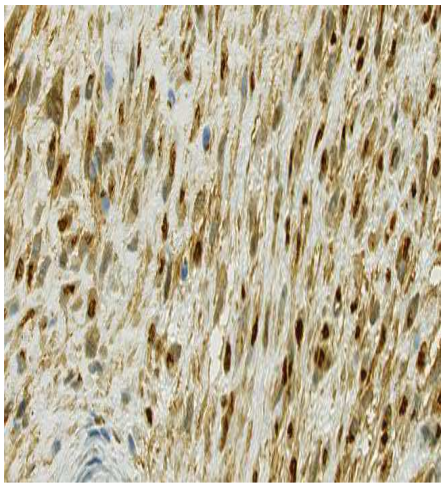
- 29 year-old woman, No past history
- Right parietal mass increasing in size (8 cm) for 5 months
- Percutaneous needle core biopsy / sonography
- Desmoïd tumor, Somatic mutation CTNNB1 T 41 A

April 2012

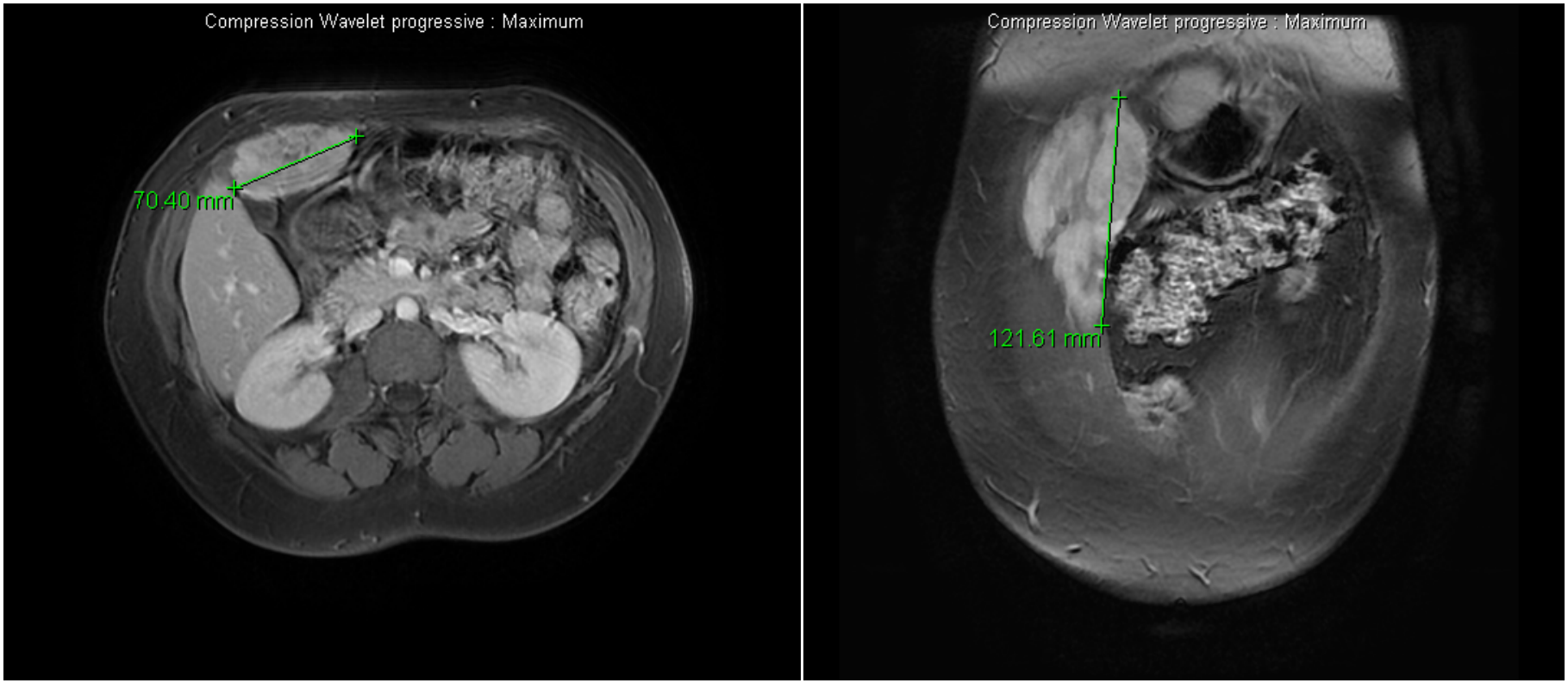




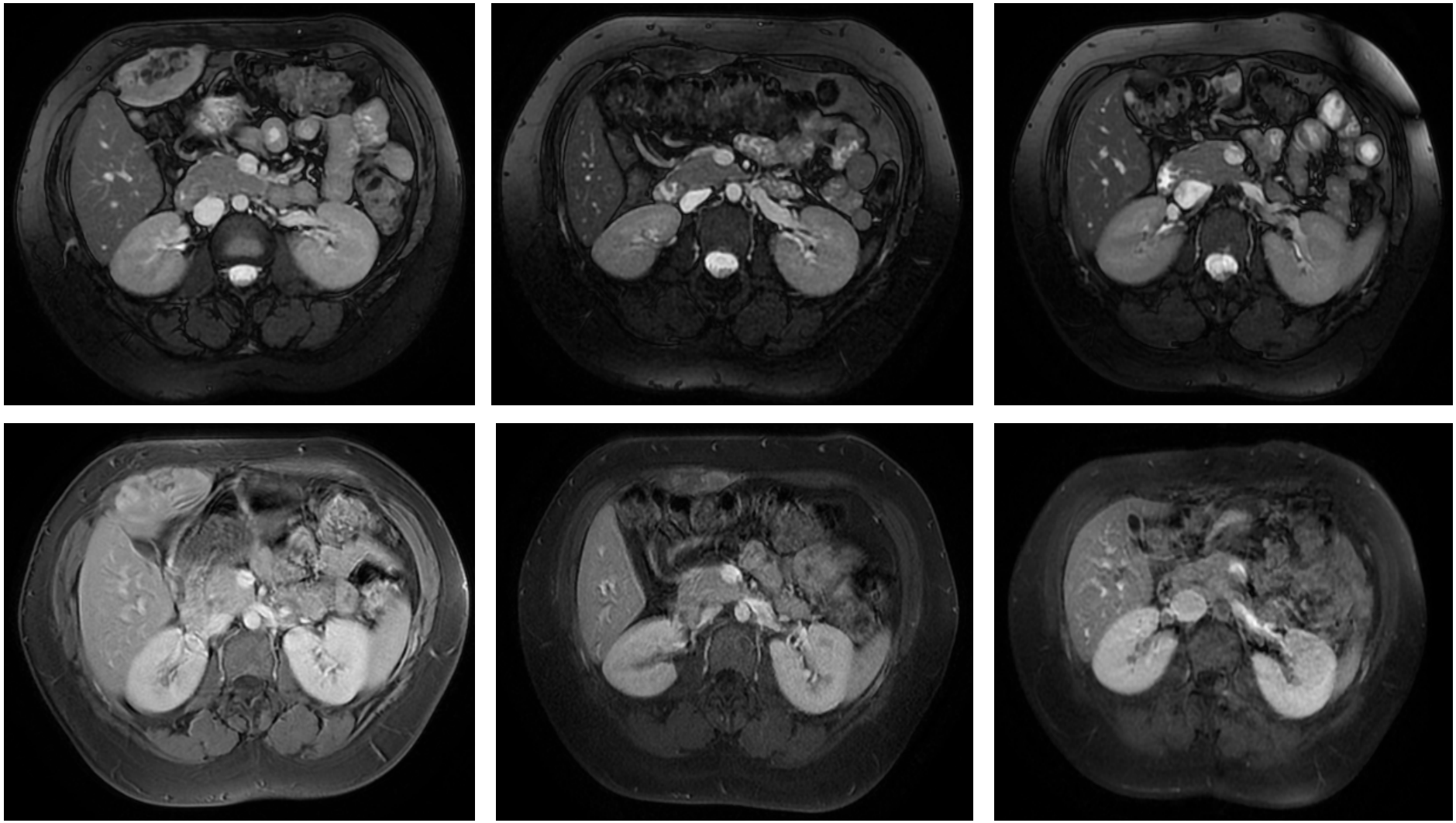




- Gave birth to a healthy baby april 2013
- Clinically: ± 12 cm mass (+50%)



April 2013 +1Year + 50%



April 2013
Delivery

November 2013

May 2014
+2 years ≈ 0

British Journal of Cancer (2011) 104, 37 – 42

www.bjcancer.com

Evaluation of management of desmoid tumours associated with familial adenomatous polyposis in Dutch patients

MH Nieuwenhuis[*,1], EM Mathus-Vliegen[2], CG Baeten[3], FM Nagengast[4], J van der Bijl[5], AD van Dalsen[6], JH Kleibeuker[7], E Dekker[2], AM Langers[8], J Vecht[9], FT Peters[7], R van Dam[3], WG van Gemert[3], WN Stuifbergen[10], WR Schouten[11], H Gelderblom[12] and HFA Vasen[1,8]

BACKGROUND: The optimal treatment of desmoid tumours is controversial. We evaluated desmoid management in Dutch familial adenomatous polyposis (FAP) patients.

METHODS: Seventy-eight FAP patients with desmoids were identified from the Dutch Polyposis Registry. Data on desmoid morphology, management, and outcome were analysed retrospectively. Progression-free survival (PFS) rates and final outcome were compared for surgical *vs* non-surgical treatment, for intra-abdominal and extra-abdominal desmoids separately. Also, pharmacological treatment was evaluated for all desmoids.

RESULTS: Median follow-up was 8 years. For intra-abdominal desmoids ($n = 62$), PFS rates at 10 years of follow-up were comparable after surgical and non-surgical treatment (33% and 49%, respectively, $P = 0.163$). None of these desmoids could be removed entirely. Eventually, one fifth died from desmoid disease. Most extra-abdominal and abdominal wall desmoids were treated surgically with a PFS rate of 63% and no deaths from desmoid disease. Comparison between NSAID and anti-estrogen treatment showed comparable outcomes. Four of the 10 patients who received chemotherapy had stabilisation of tumour growth, all after doxorubicin combination therapy.

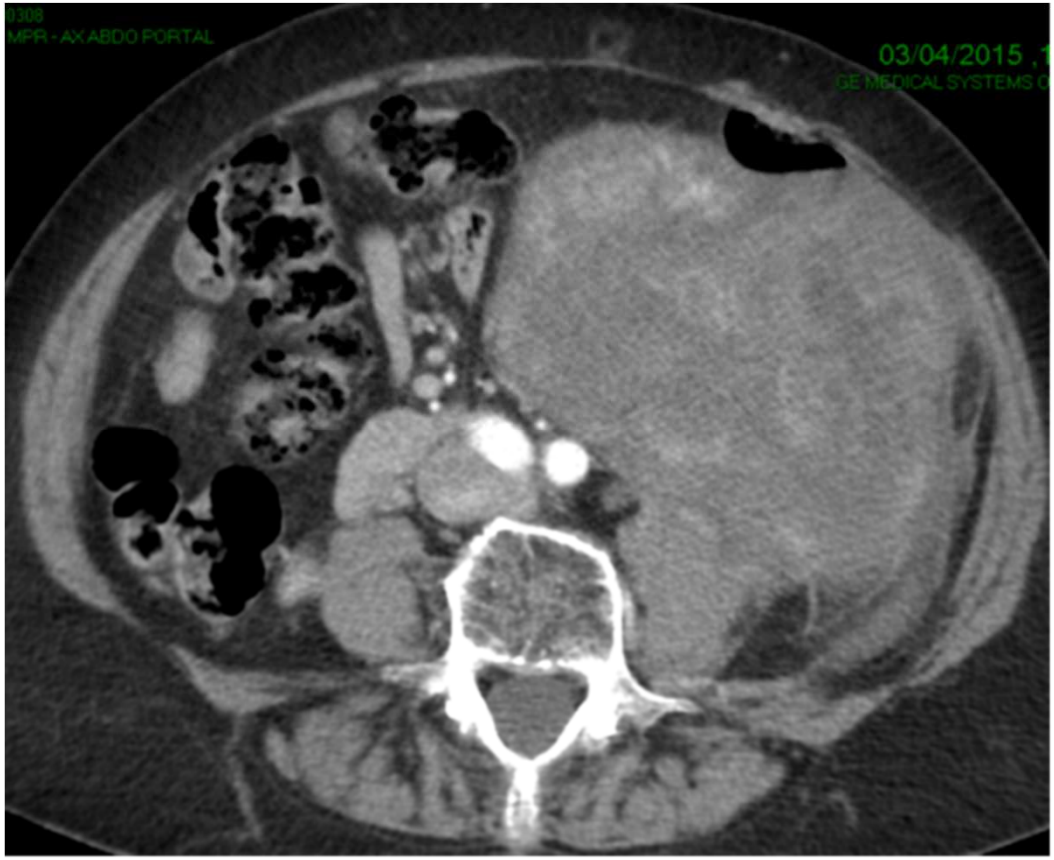
CONCLUSION: For intra-abdominal desmoids, a conservative approach and surgery showed comparable outcomes. For extra-abdominal and abdominal wall desmoids, surgery seemed appropriate. Different pharmacological therapies showed comparable outcomes. If chemotherapy was given for progressively growing intra-abdominal desmoids, most favourable outcomes occurred after combinations including doxorubicin.

British Journal of Cancer (2011) **104,** 37 – 42. doi:10.1038/sj.bjc.6605997 www.bjcancer.com
Published online 9 November 2010

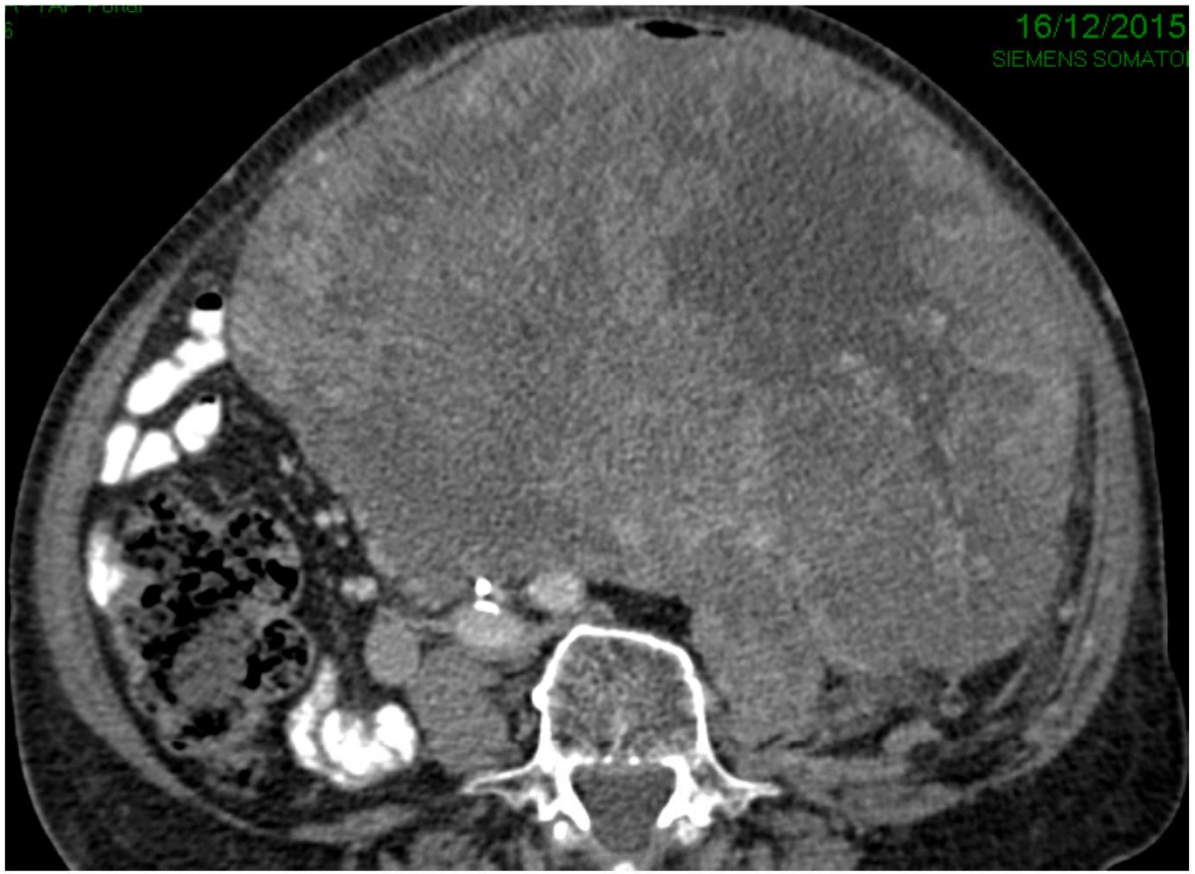
CONCLUSION: For intra-abdominal desmoids, a conservative approach and surgery showed comparable outcomes.

Best indications after progression

- February 2015: self palpation abdominal mass
  May 2015 percutaneous biopsy: desmoid



June -august 2015: TAM
August-december 2015: Navelbine …Votrient
December 2015:Consultation Curie



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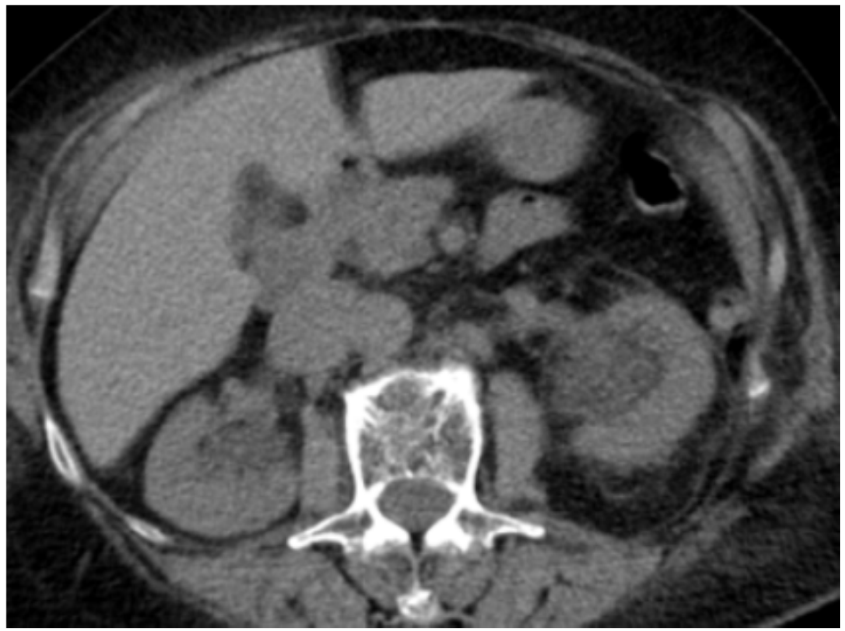
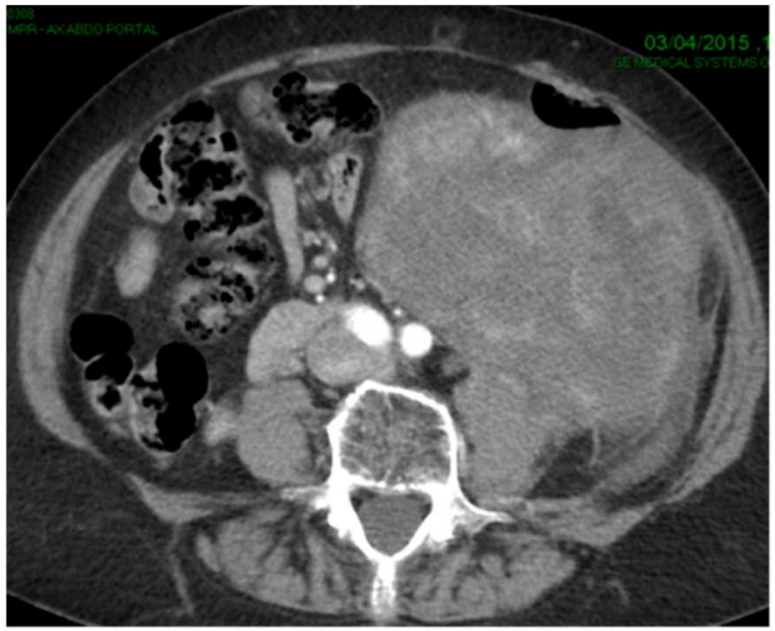
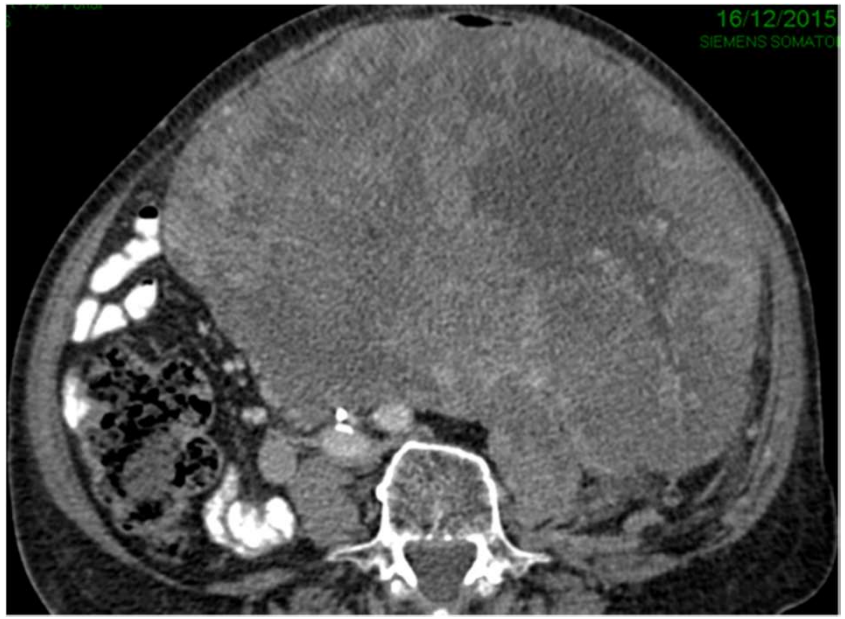
Ensemble, prenons le cancer de vitesse.

September2014

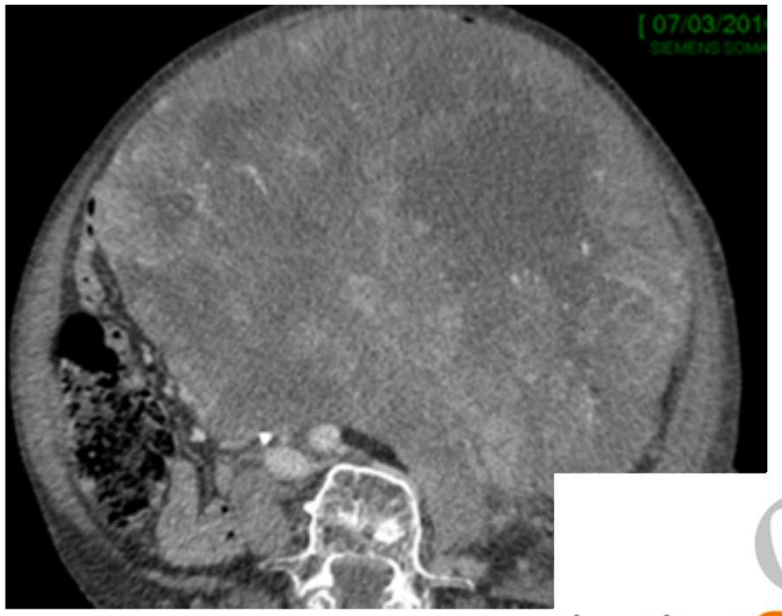


Avpil 2015





December 2015



March 2016

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Ensemble, prenons le cancer de vitesse.

European Journal of Cancer 58 (2016) 90–96

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Management of desmoid tumours: A nationwide survey of labelled reference centre networks in France☆

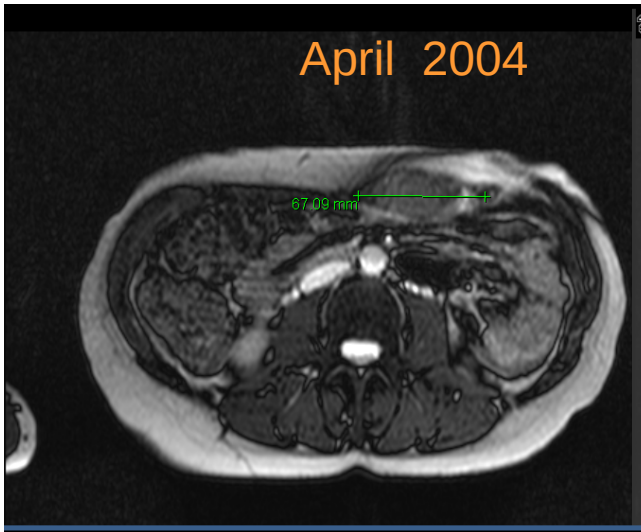
Nicolas Penel [a,b,*], Jean-Michel Coindre [c], Sylvie Bonvalot [d,e], Antoine Italiano [f], Agnès Neuville [c], Axel Le Cesne [g], Philippe Terrier [h], Isabelle Ray-Coquard [i], Dominique Ranchere-Vince [j], Yves-Marie Robin [k], Nicolas Isambert [l], Gwennaël Ferron [m], Florence Duffaud [n], François Bertucci [o], Maria Rios [p], Eberhad Stoeckle [q], Cécile Le Pechoux [r], Cécile Guillemet [s], Jean-Baptiste Courreges [t], Jean-Yves Blay [i]

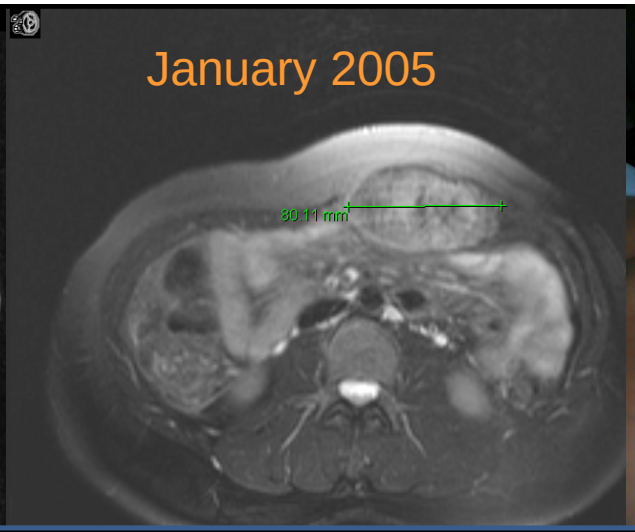
- 2010 to 2013, expert pathologists of FSG confirmed the diagnosis of DT in 861 pts
- 445 pts initially diagnosed outside the referral centers, were reviewed
- Prior to the review, DT was diagnosed in 389/545 cases (71·3%)
- 156/545 cases (28·7%) had another diagnosis
- The most common misdiagnoses were:

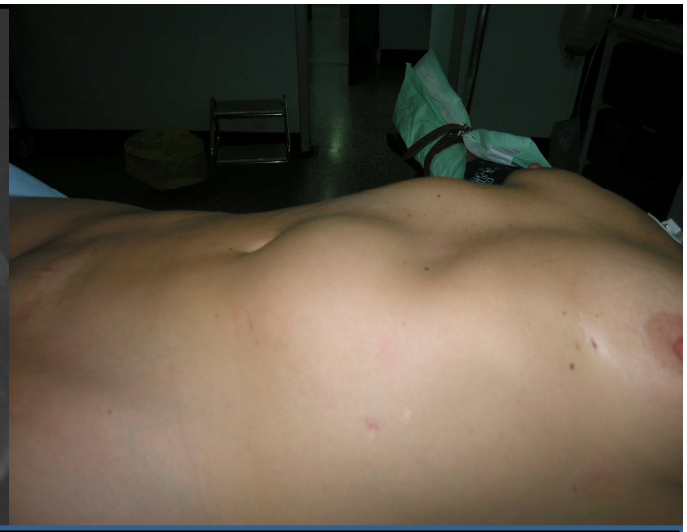
- sarcoma in 35/156 cases (22·4%)
- GIST in 26/156 cases (16·6%)
- nodular fasciitis 20/156 cases (12·8%)
- leiomyoma 6/156 cases (3·8%)

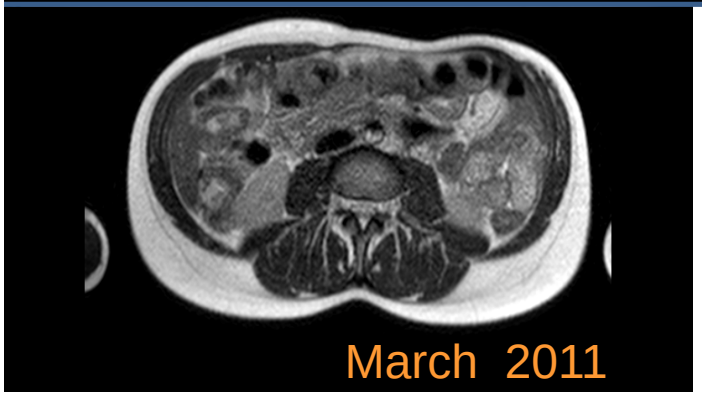
Best indications of surgery after progression

- **Abdominal/thoracic wall**
- **Limb when no anatomical constraints**
- **Intra-abdominal: when limited small intestine resection**

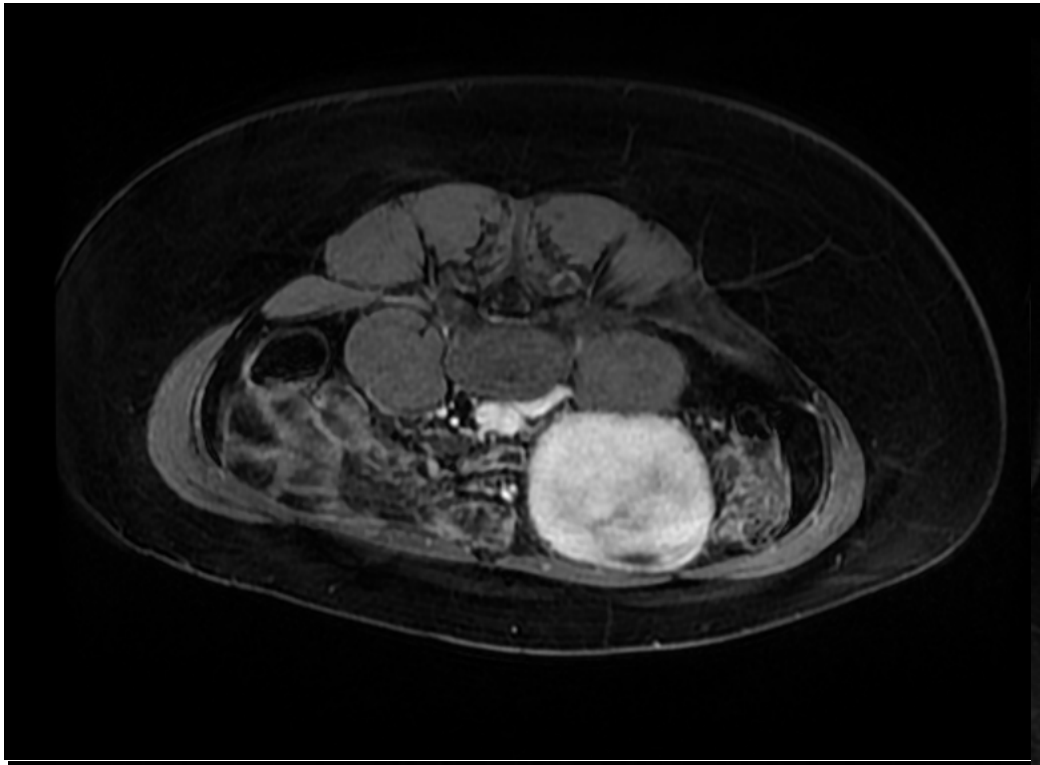


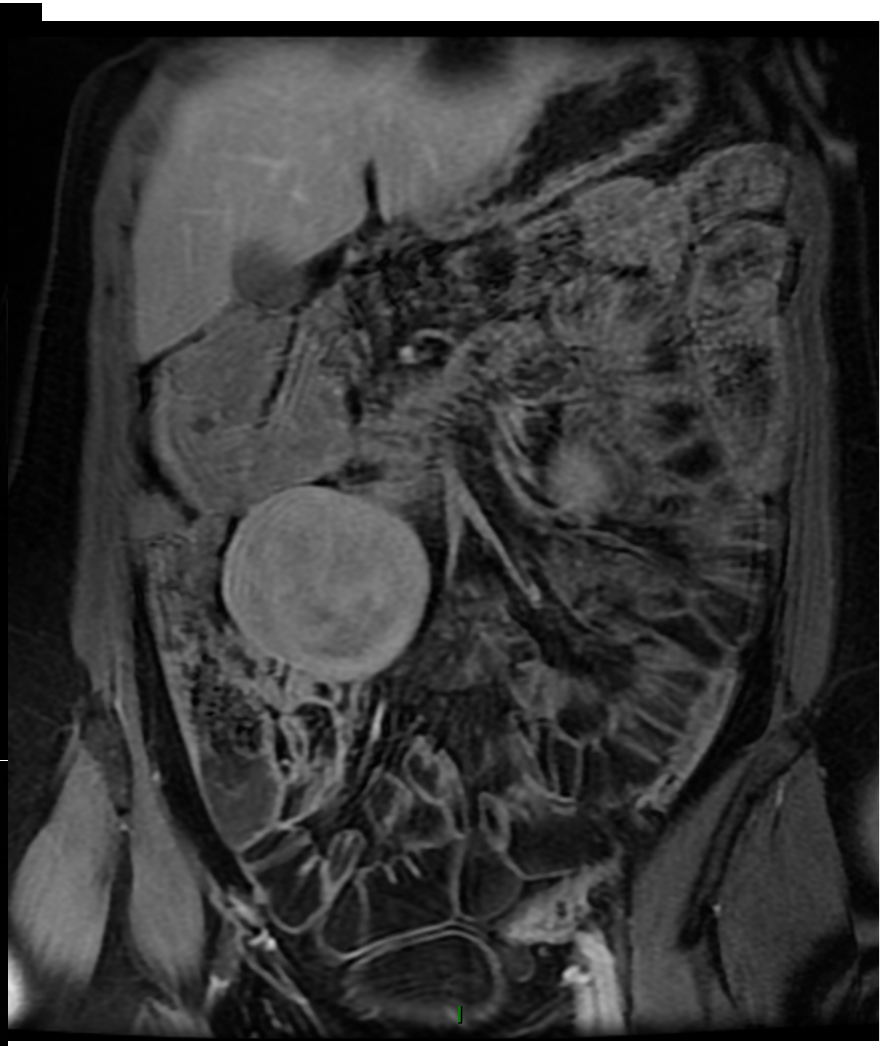


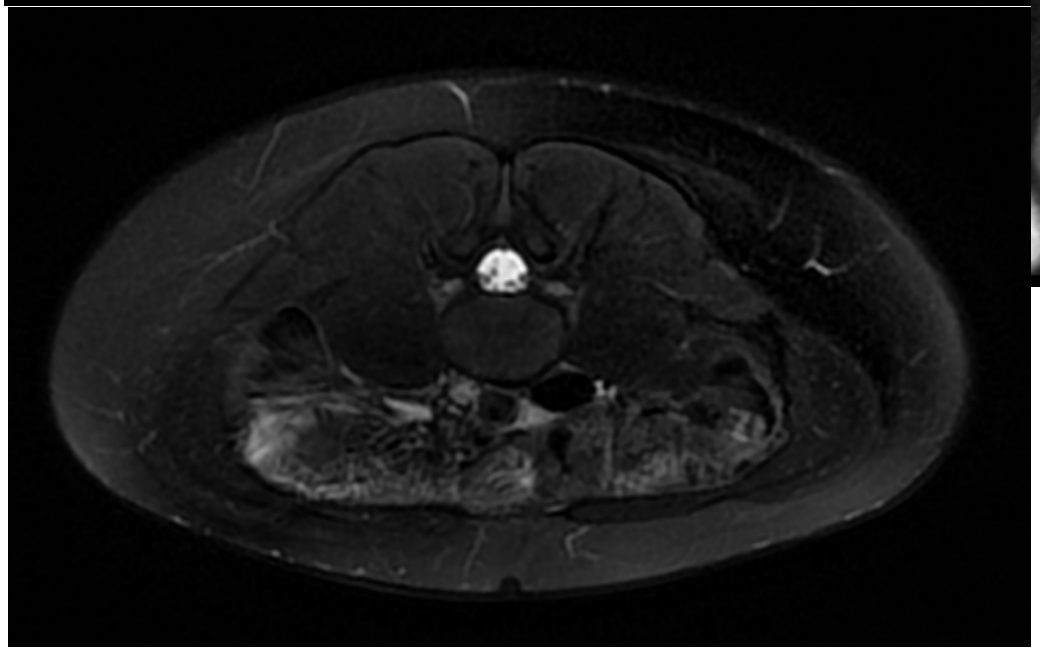




- 31 years old female
- AF (biopsy)
- Evolutive after 9 months including 6 mths TAM
- Parietectomy

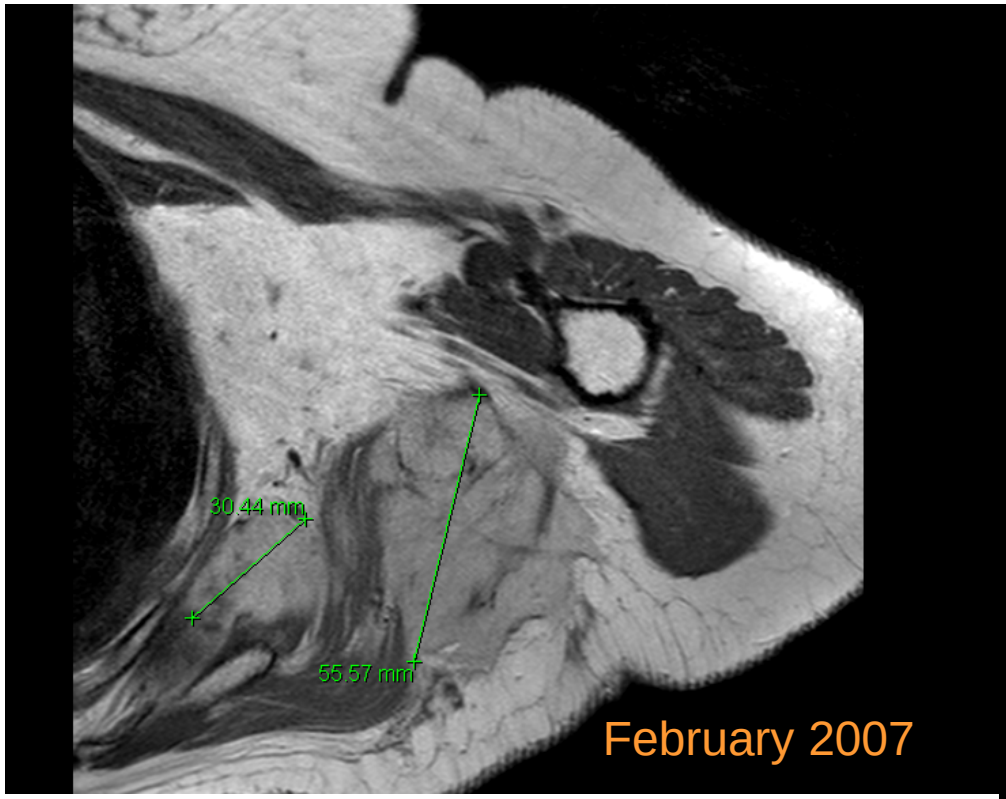




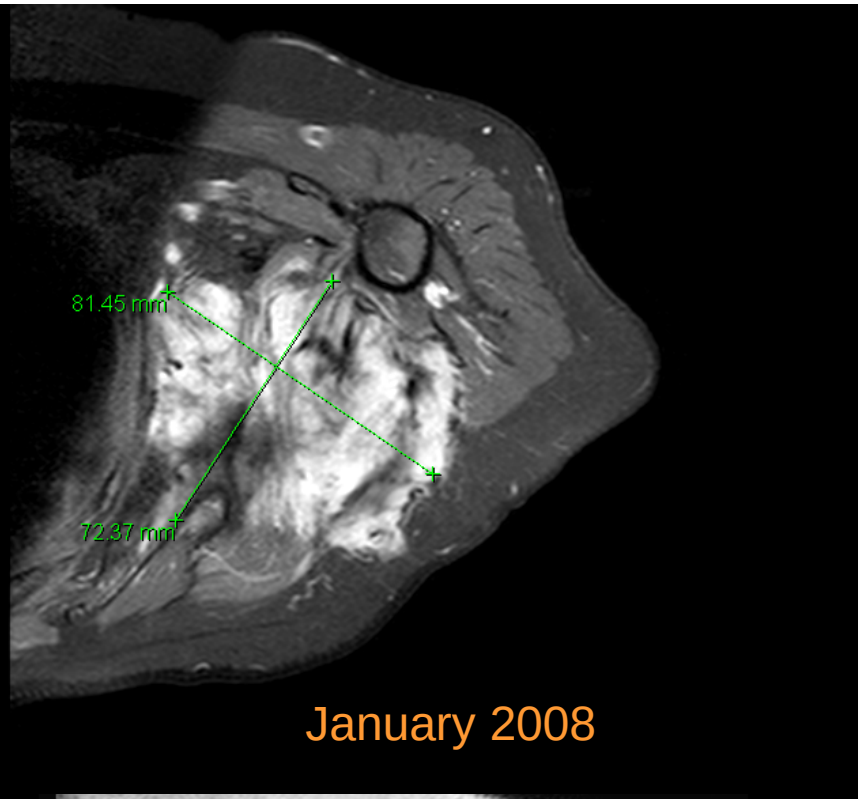


Best indications of radiotherapy after progression

- **Girdle**
- **Head and neck**
- **Back**
- **Limb when anatomical constraints**

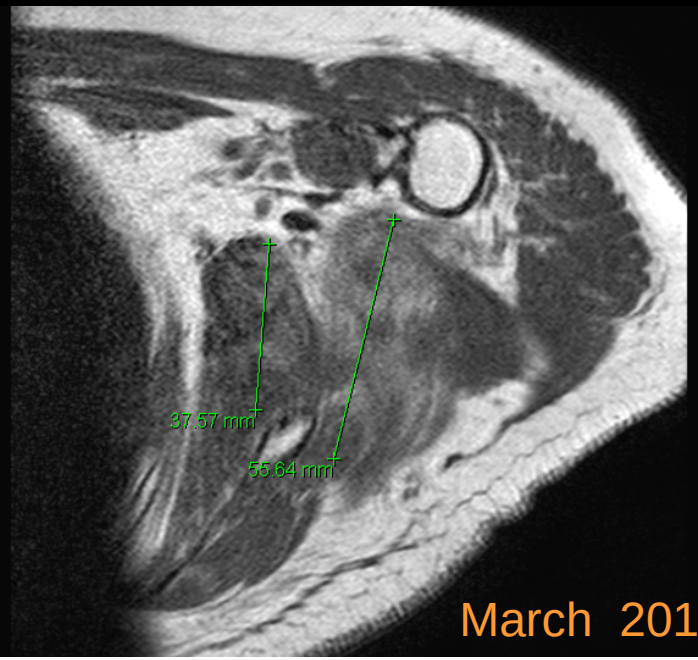


February 2007



January 2008

Female 59 years old
Surgical biopsy: desmoid
Initial wait and see
Progression
Exclusive radiotherapy 60 Gy



March 2015

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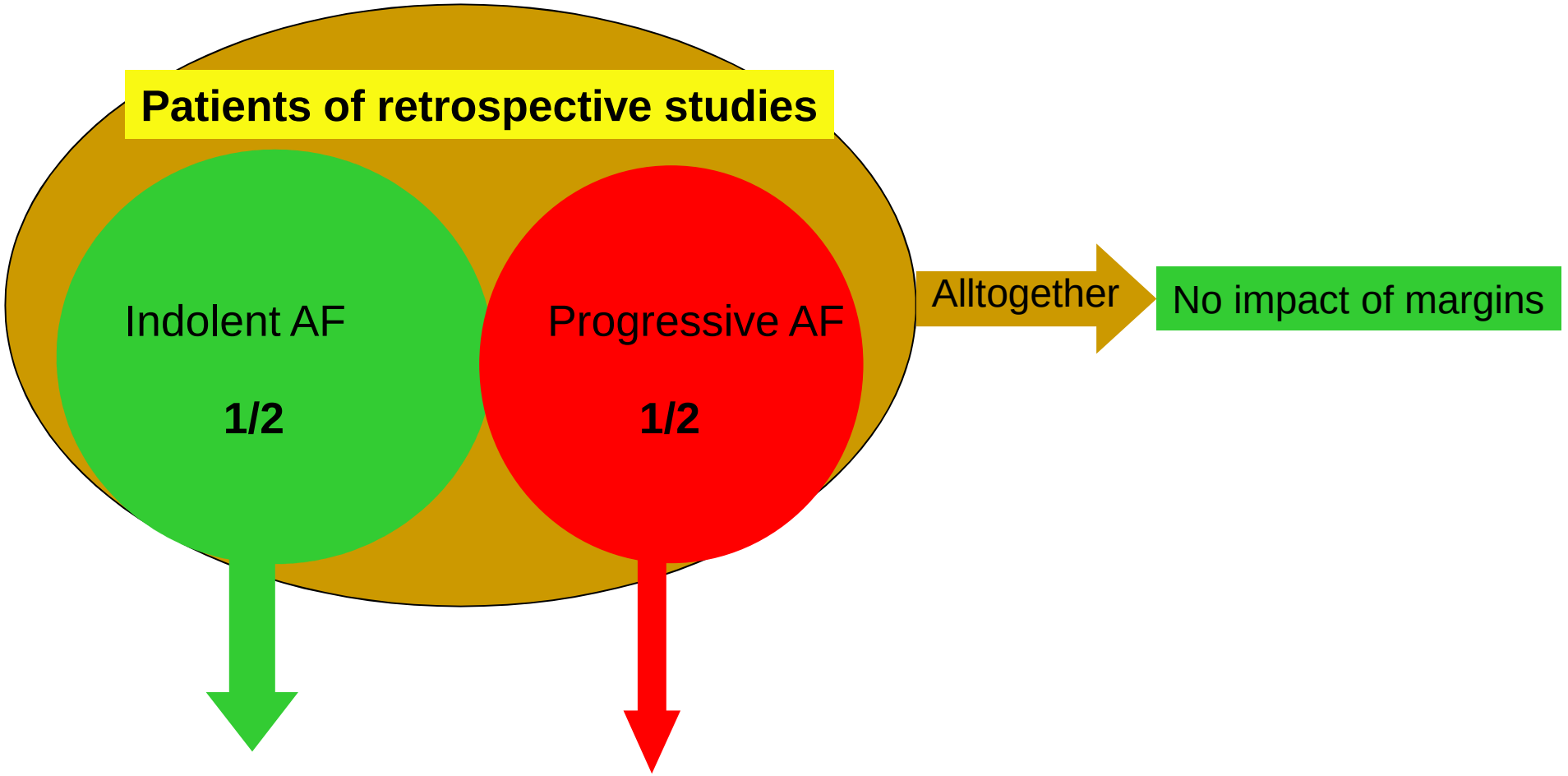
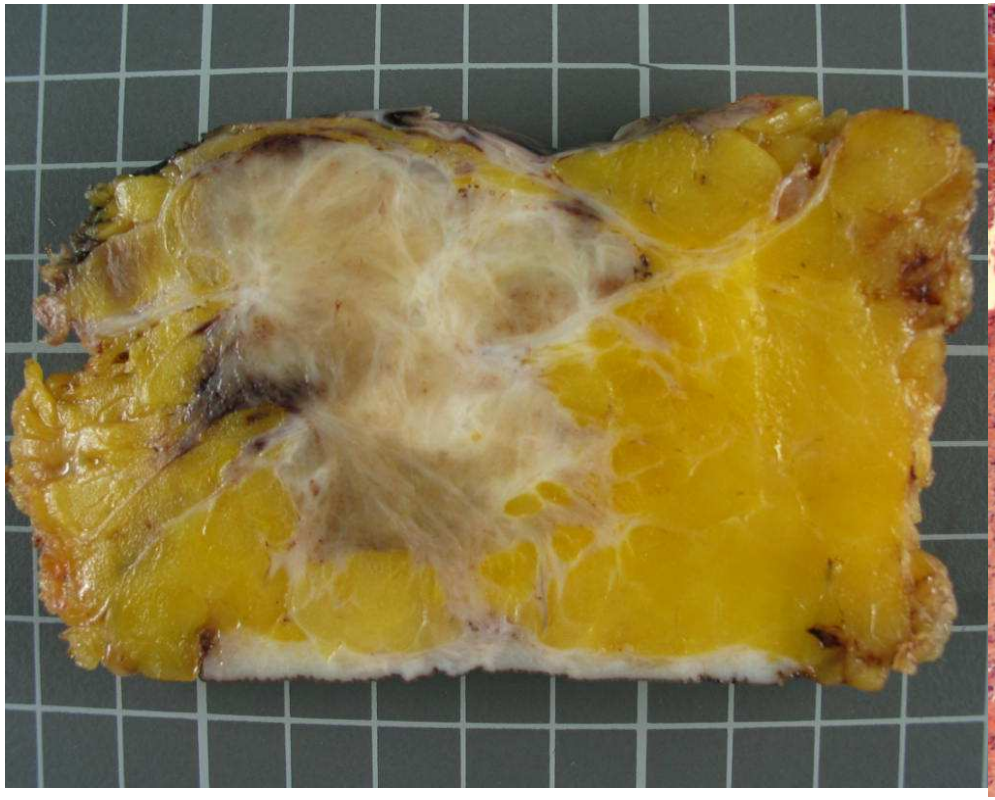
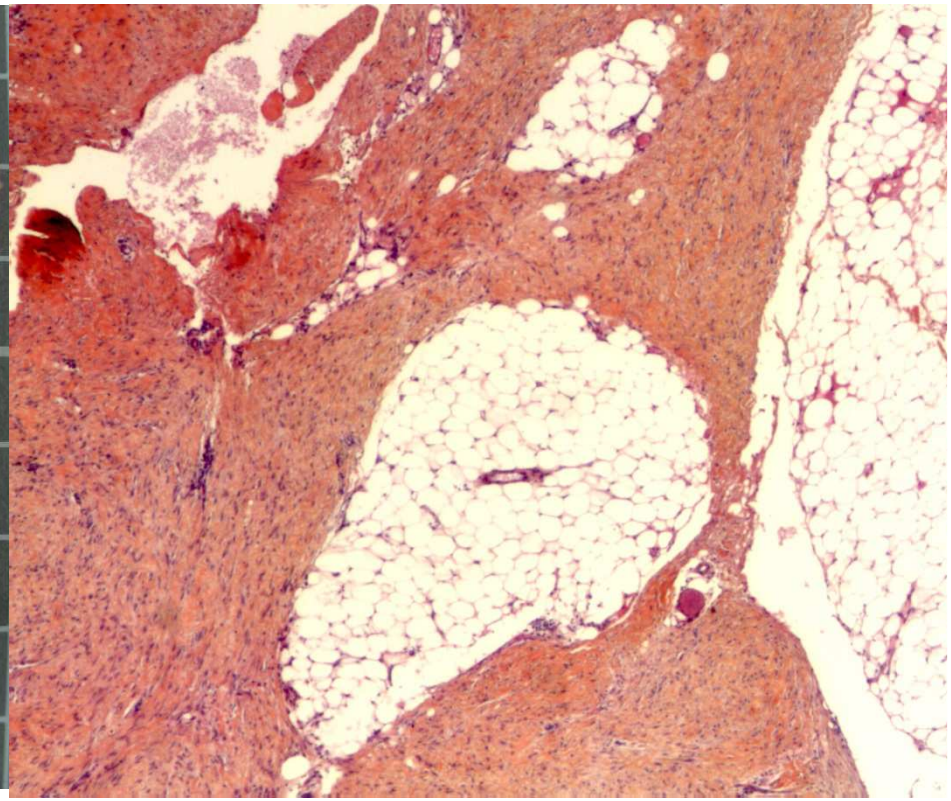
Surgery: how??

- Margins
- Reconstructions
- ILP

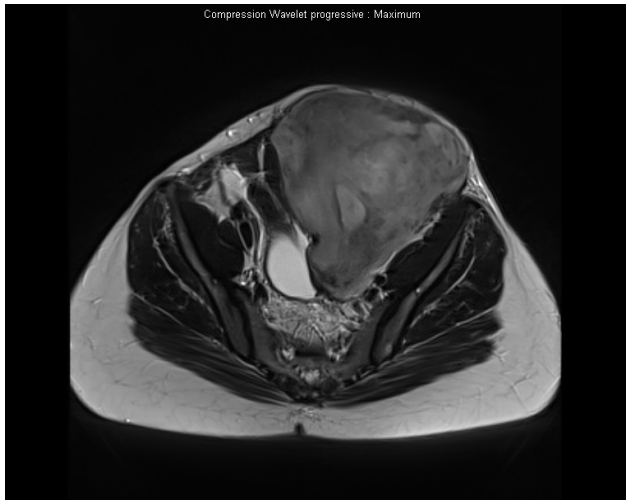

Patients of retrospective studies
Indolent AF
1/2
Progressive AF
1/2
Alltogether
No impact of margins
No impact of margins
All treatments will be efficient
No treatment could be enough
Negative impact of positive margins
Need for adapted treatment

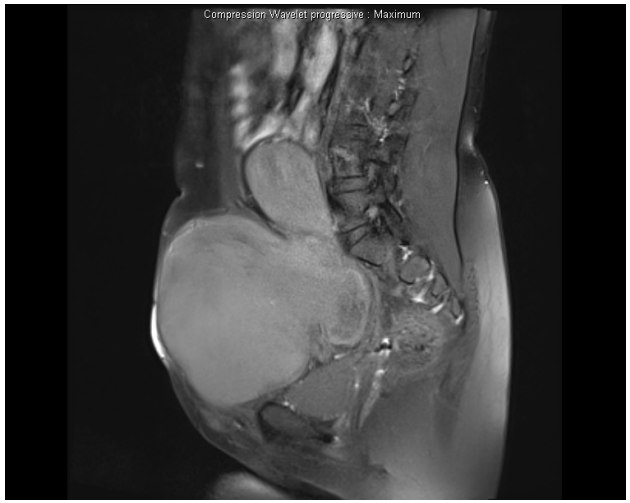


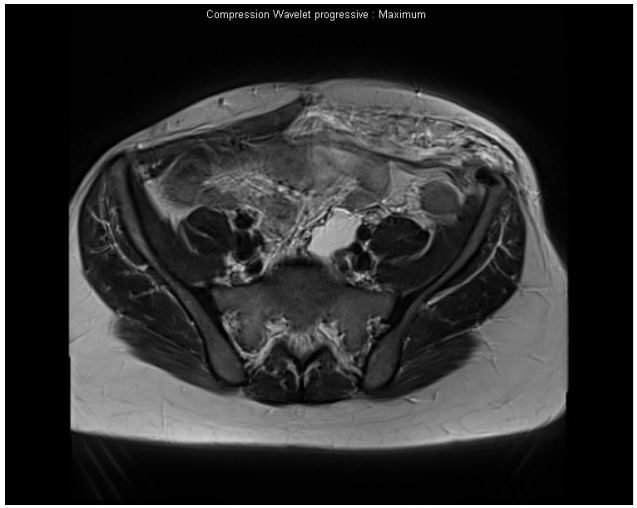


Desmoide

Surgery and Reconstruction







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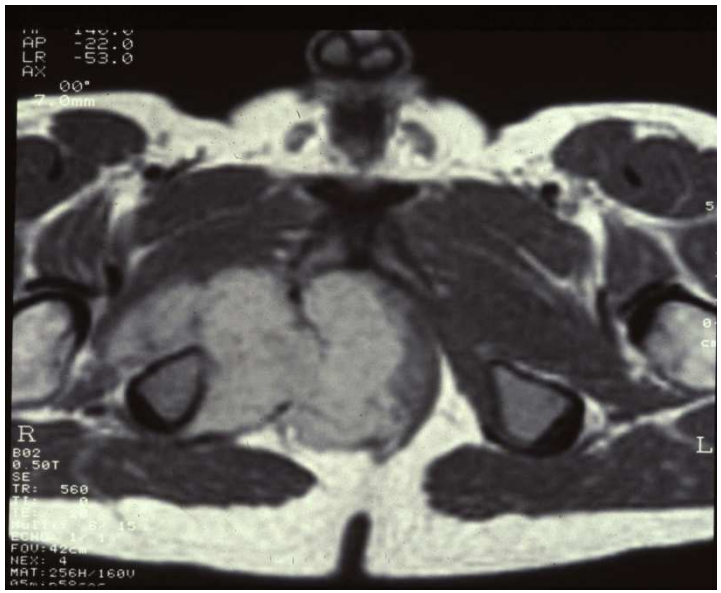
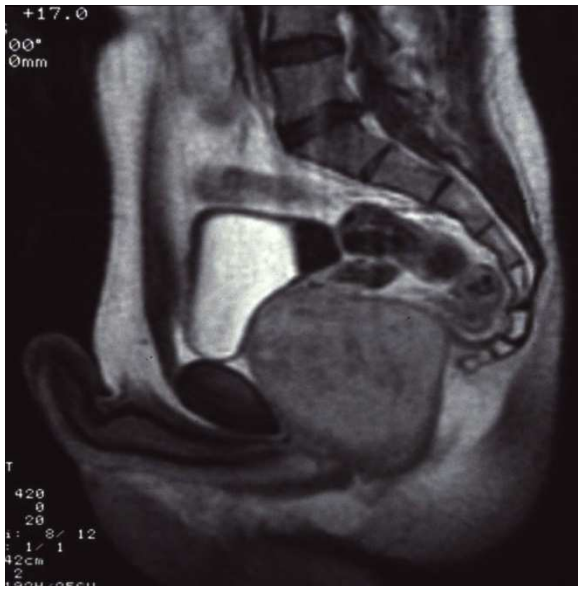
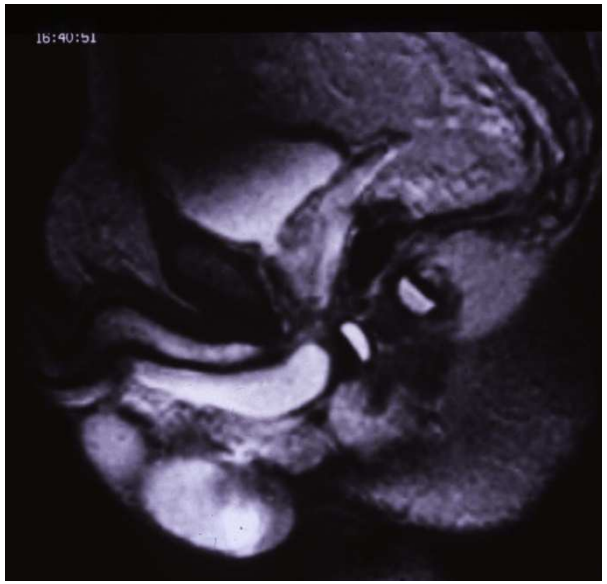
Surgery and Reconstruction







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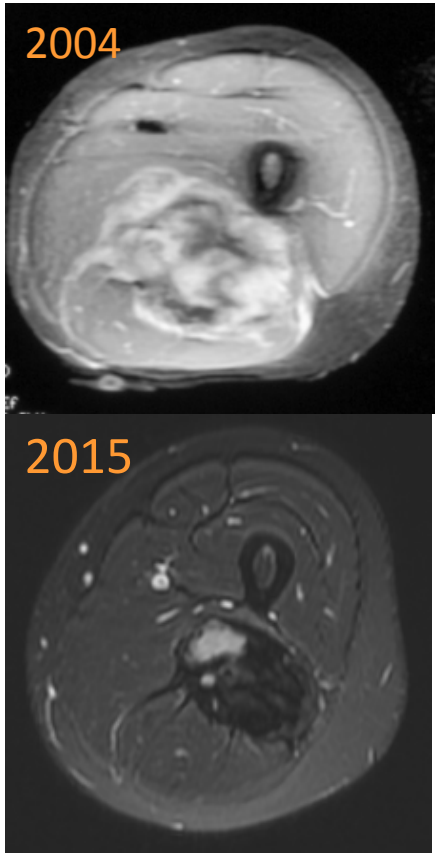
Isolated limb perfusion with tumor necrosis factor-alpha and melphalan has a possible role

	N	CR	PR	Stable	Local progression
Lev- chelouche (Surgery 1999)	6	2	3		2 (Follow up 45 months)
Bonvalot (Ann Surg Oncol 2010)	8	1	6		1 (Follow up 27 months)
van Broekhoven (BJS 2014)	25	2	16	7	Amputation 3 pts (Follow up 84months)



20 years old Female Fibromatosis of the thigh

Etude WS

- PHRC
- 100 pts déjà inclus/100 prévus
- Attente follow up 3 ans
- Résultats en 2018

Conclusions

- Patients with diagnosis doubt, complication (occlusion, perforation…), or cosmetic issue should be operated at first
- After progression, best indication of surgery are Abdominal/thoracic wall, Intra-abdominal T and limb when there is no anatomical constraints
- Objective should be complete resection
- Reconstructions must be planned up front

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