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# Extraskeletal Osteosarcoma: Clinico-pathologic Features and Results of Multimodal Management

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# Extraskeletal Osteosarcoma: Clinico-pathologic Features and Results of Multimodal Management

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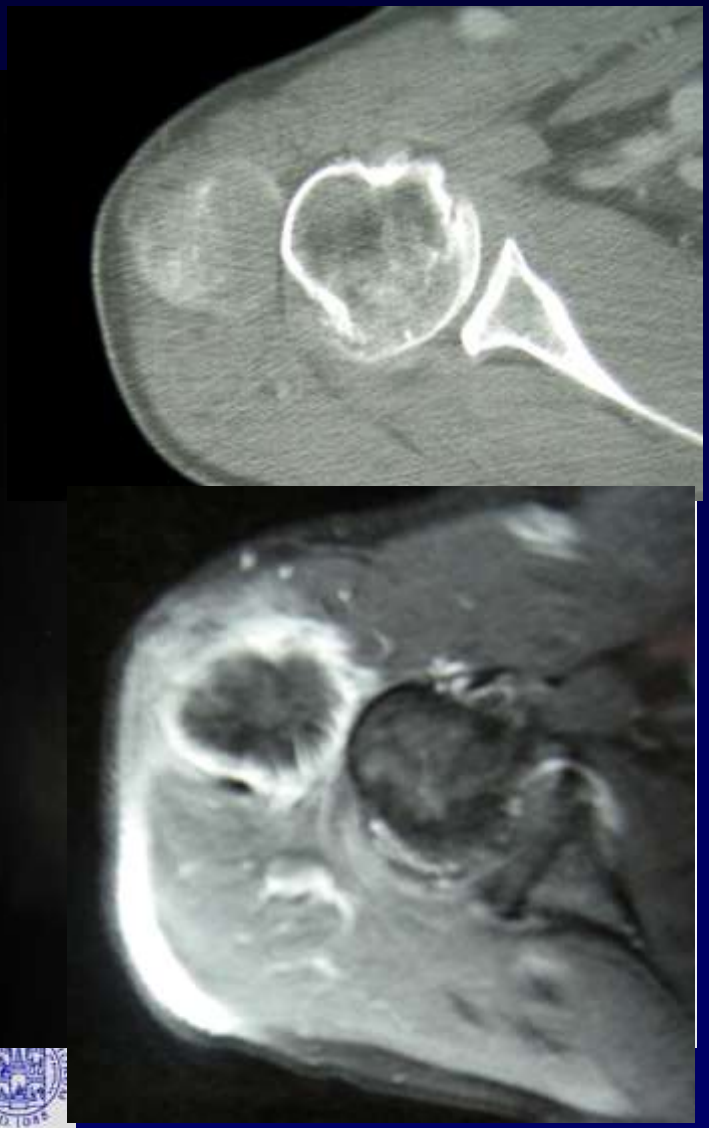
# Background

- About 1% of all soft tissue sarcomas
- First described by Wilson in 1941
- Few large series then reported
- Older individuals & usually worse survival than skeletal osteosarcoma

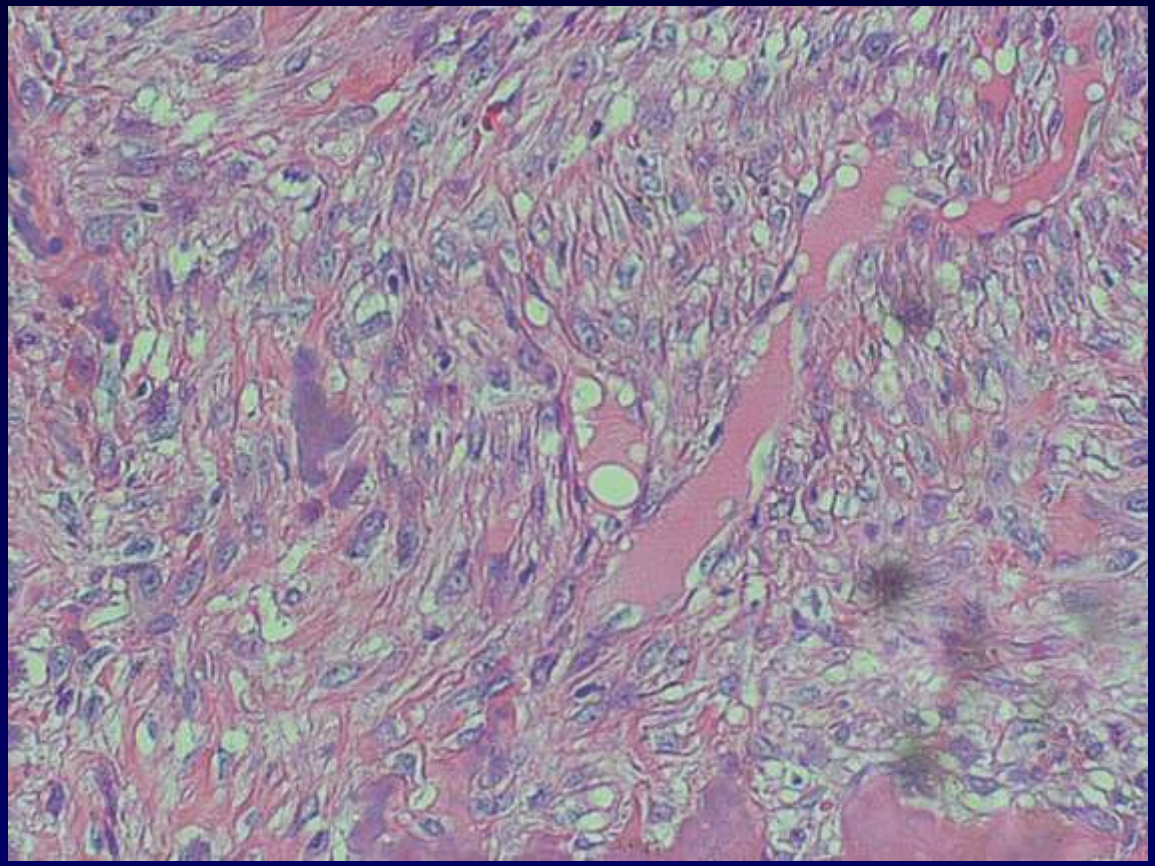
# Diagnostic Criteria



- Arise in the soft tissue and not be attached to bone/periosteum

*Extraskeletal Osteosarcoma*

# Diagnostic Criteria



- Uniform sarcomatous pattern, high-grade
- Produce osteoid-bone/cartilage matrix

# Classic Literature: 80's-90's

- 26-88 pts, 1915-1988, all high-grade lesions
- Mean age 51-55 yrs, M:F=1-1.9, 47-68% lower limb
- Mgmt: mostly surgical unimodal, little role for Rxt/Cht
- LR 43-69%, mets 61-80%, 5yr OS rate 24-37%
- Suggested role for tumor size, surgical margin and possibly aggressive multimodal management

*MSKCC - Sordillo PP et al, Cancer, 1983*
*AFIP - Chung EB & Enzinger FM, Cancer, 1987*
*MDACC - Bane BL et al, Cancer, 1990*
*Mayo Clinic - Lee JS et al, Cancer, 1995*

*Extraskeletal Osteosarcoma*

# Recent Literature

- 17-38 pts, 12-20 yrs experience, all high-grade lesions
- Mean age 44-55 yrs, M:F=1-2, 47-52% lower limb
- Mgmt: mostly multimodal - Surgery & Cht, less Rxt
- LR 16-29%, mets 7-39%, 3yr EFS 56%, 5yr EFS 47% 5ys OS rate 46-66%
- Improved outcome, better surgical margin, Cht likely beneficial even if questionable clin/path response

*MDACC - Ahmad SA et al, J Clin Oncol, 2002*

*Munster - Goldstein-Jackson SY et al, J Cancer Res Clin Oncol, 2005*

*Japan, multicentric - Torigoe T et al, J Orthop Sci, 2007*

# Rizzoli Experience

- 48 pts, 1966-2007, 36 admitted, 12 consults
- Clinico-path & radiologic features reviewed
- Management correlated with outcome
- Updated FU obtained in all patients
- Kaplan Meier & log rank survival analysis

# Rizzoli Experience

- Median age 53.6 yrs, M 21/F15, LL 69%
- Prox 52.8%, Distal 16.7%, Girdles 30.6%
- All high-grade lesions; def Dx on specimen 16 (44%)
- 23 pts localised (64%), 13 metastatic (36%)
- 16 prev. excision admitted for further surgery

# Rizzoli Experience: Management

- Surgery: 34 (LS 69.5%, amp 25%), 2 inop.
- Margins: adequate 76.5%, inadequate 23.5%
- Cht 19 (52.8%): 17 adjuv postop, 2 neoadjuv
  - 2 to 4 drugs regimen based on pt age
- Postoperative Rxt: 6 patients (16.7%)

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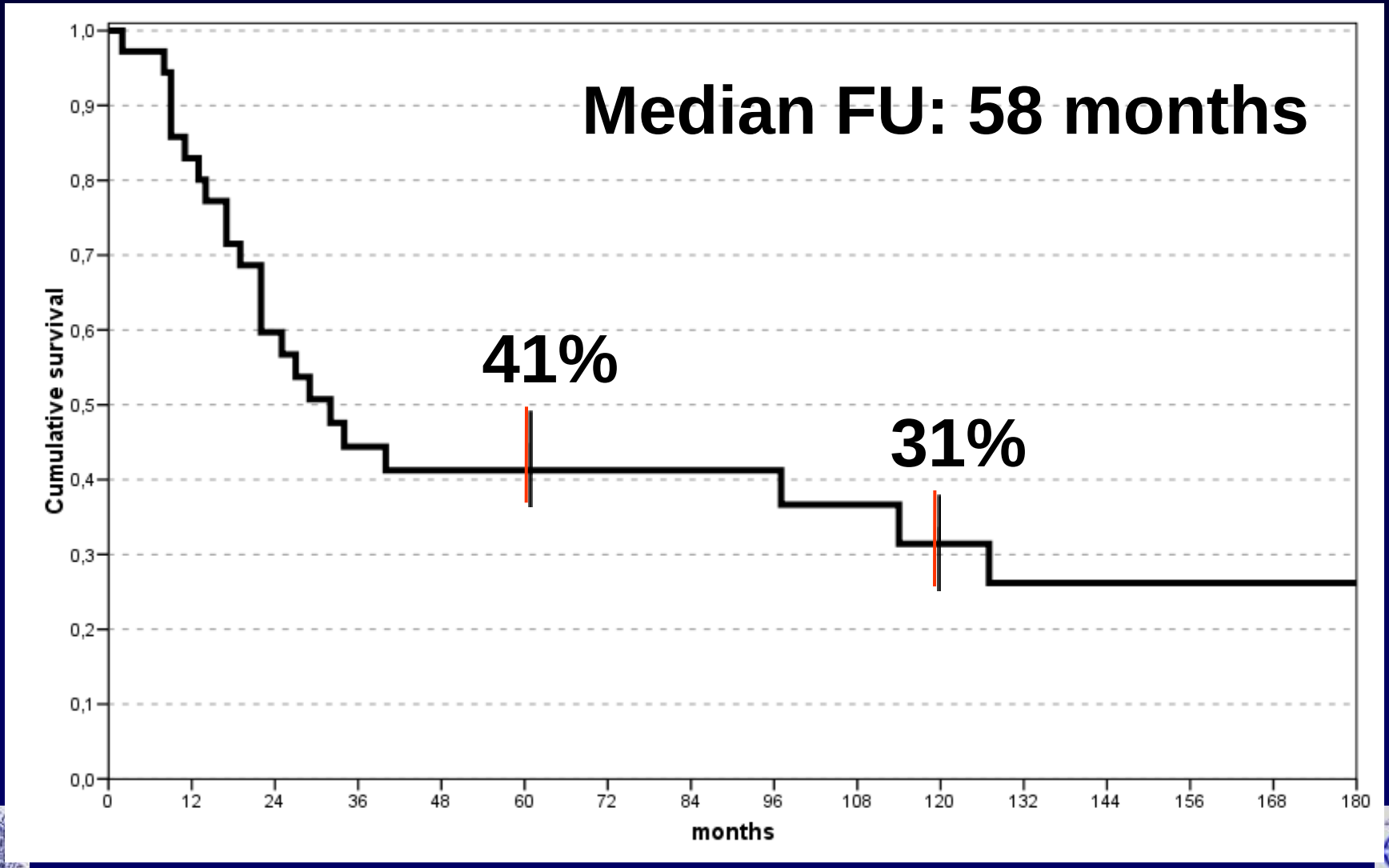
# Expected Overall Survival



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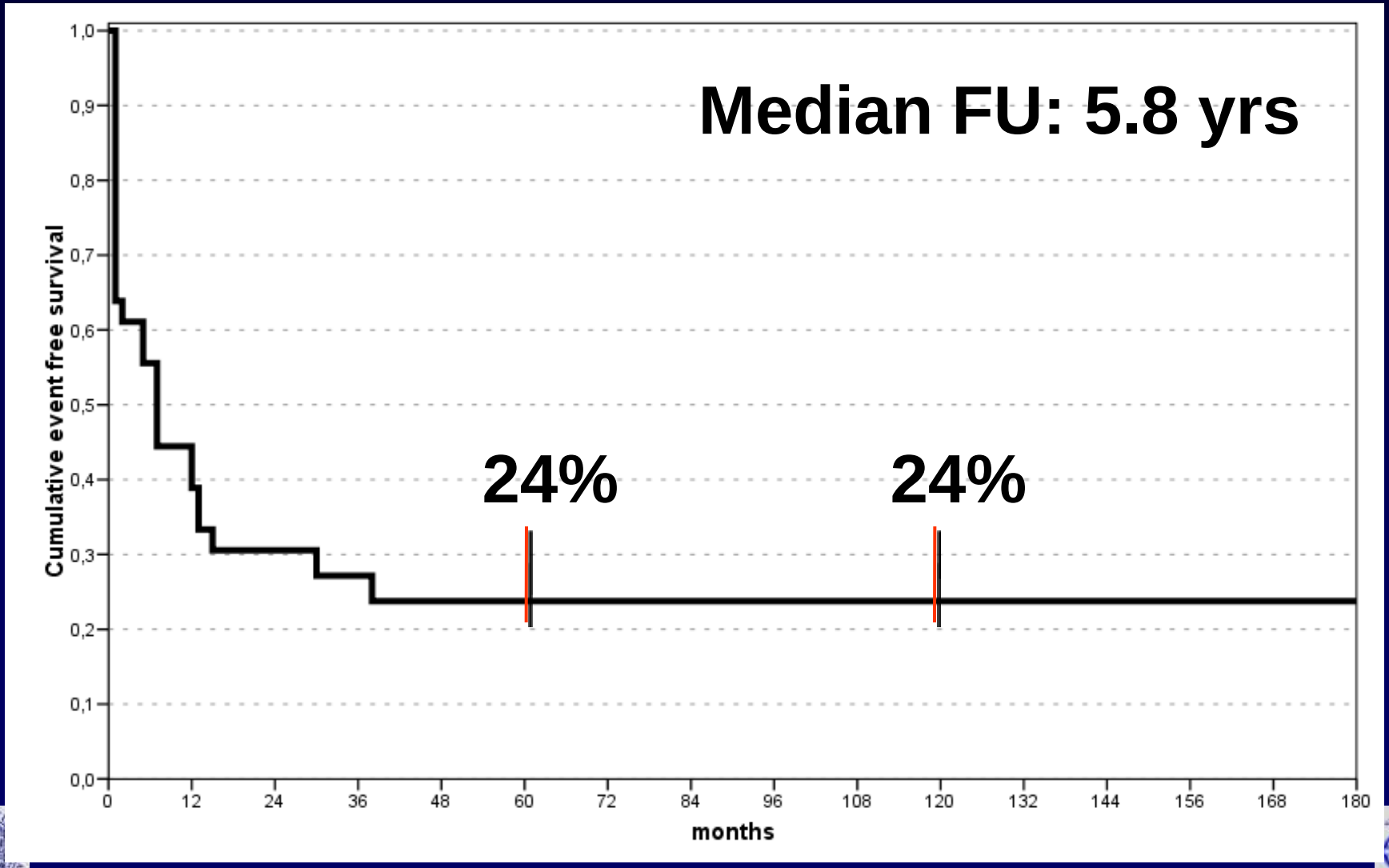
# Expected Event-Free Survival



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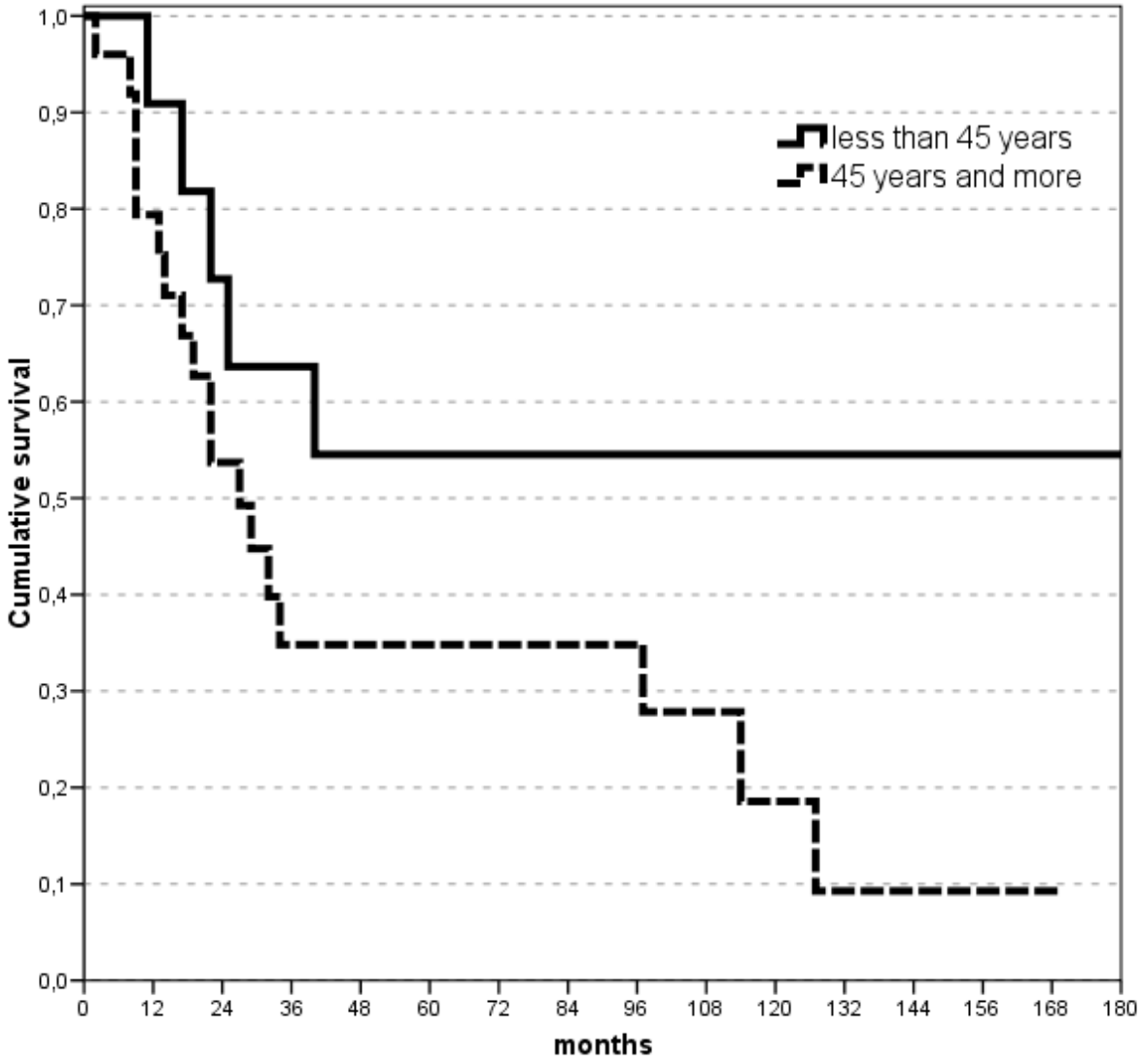
# Overall Survival: Age




***p=0.066***

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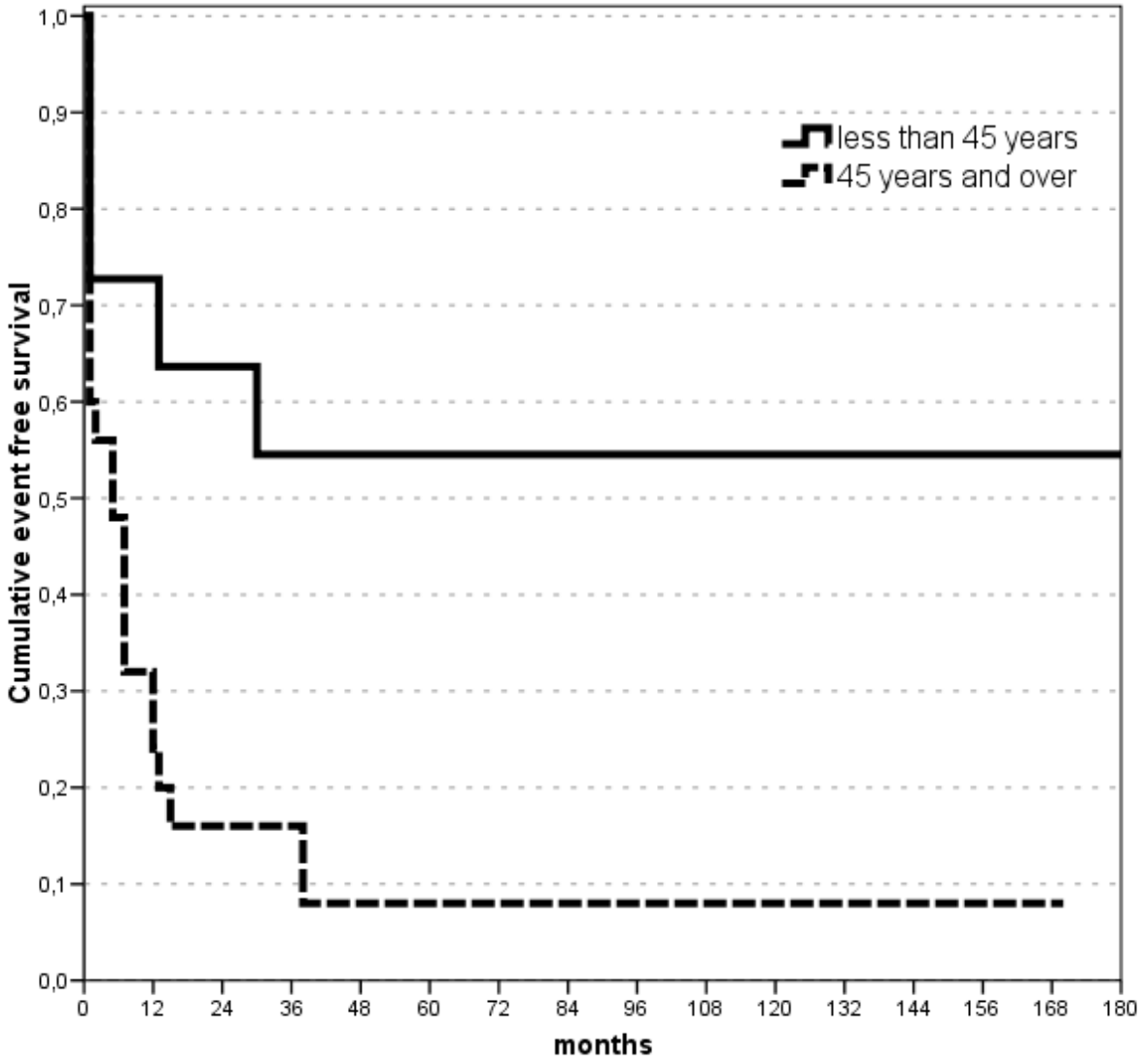
# Event-Free Survival: Age




***p=0.007***

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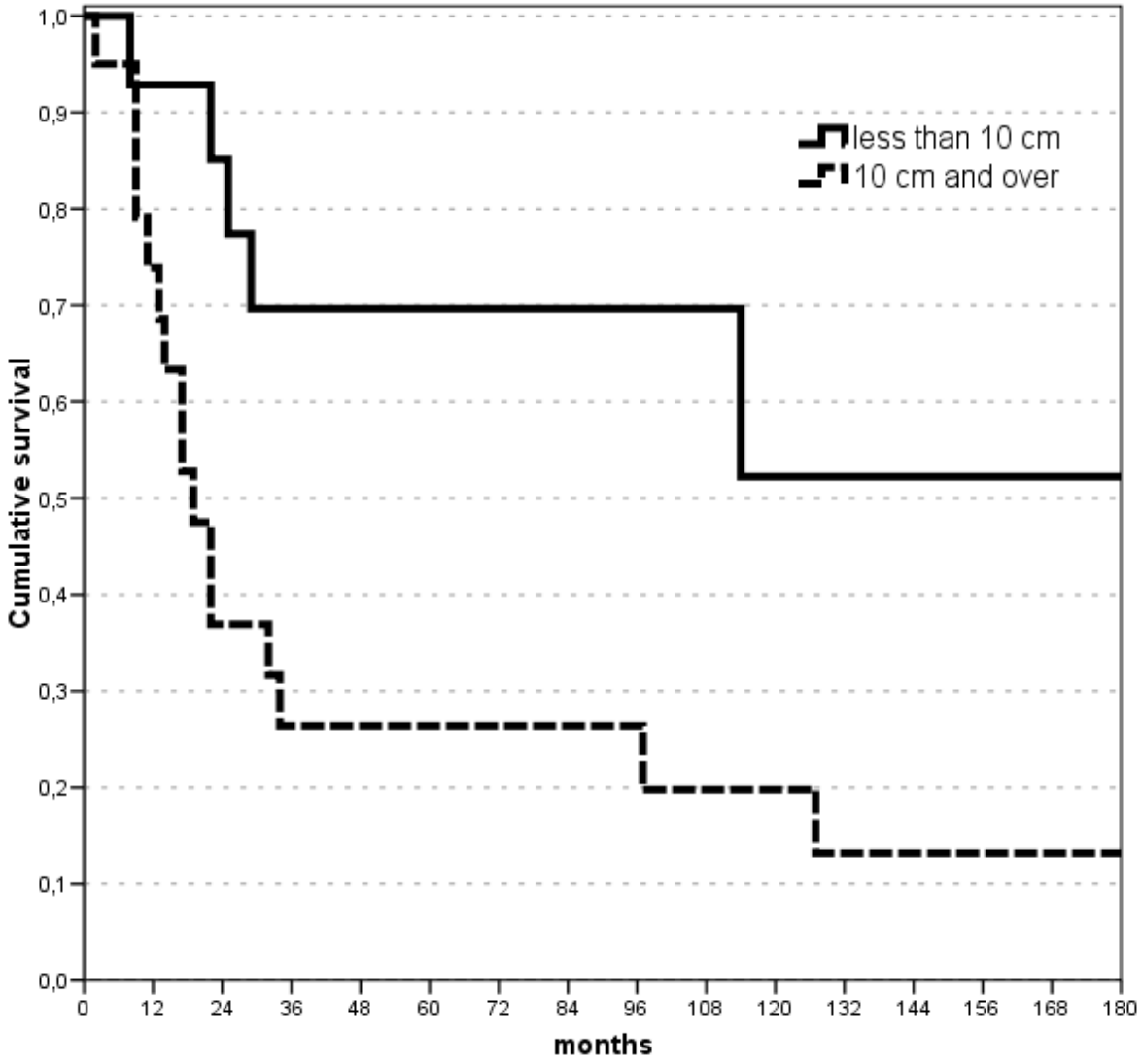
# Overall Survival: Tumor Volume




***p=0.01***

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# Overall Survival: Stage

- 23 pts localised, 9 survivors (1DOC when DF)
  - DS survival 43.5% (DFS 39%)

NS

- 13 pts metastatic, 3 survivors (2 AWD, 1 DF)
  - DS survival 23% (DFS 7.7%)

# Overall Survival: Margin and LR

- Localised 23, operated 22
  - Adequate 18, survivors 8, DFS 44.4%
  - Inadequate 4, survivors 2, DFS 50%
  - Amputation vs LS: no difference

NS

- 8 pts developed 12 LR's ⟶ further surgery
  - 2 pts DF at final FU: 25%

# Overall Survival: Chemotherapy

- Cht: 19 pts, 8 survivors (42.1%)

NS

- No Cht: 17 pts, 5 survivors (29.4%)

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# Overall Survival: Chemotherapy

- Localised (23 pts) → improved DFS
  - Cht 10 pts: DFS 60%
  - No Cht 13 pts: DFS 31% (23%)

***p=0.09***

- Metastatic (13 pts)
  - Cht 9 pts: 1DF, 1 AWD DFS 11%
  - No Cht 4 pts: 1 AWD DFS 0%

NS

# Conclusions

- Results comparable with recent literature
- Age and volume important factors
- Worse prognosis than bone OGS ?
- Biologic behavior of aggressive STS
- Cht seems valuable in pts with loc. disease

*N. Fabbri*

*23rd EMSOS Meeting*

*Birmingham, UK*

*5th-7th May 2010*

# Literature

- *Sordillo PP et al, Cancer, 1983 - MSKCC*

  - 48 pts, 1950-1982, all high-grade lesions

  - Mean age 51 yrs, M=F, 54% lower limb, 5 prev Rxt

  - Mgmt (45 pts): Surgery 43, Cht in 5 relapses

  - LR 69%, mets 80%, LR &/or mets 91%, OS 24%

  - Survivors: amput/resection & Rxt, 4/5 Cht at relapse

# Literature

- *Chung EB & Enzinger FM, Cancer, 1987 - AFIP*

  - 88 pts, 1946-1982, all high-grade lesions
  - Mean age 54.6 yrs, M 58%, 46.6% lower limb
  - Management: unimodal (surgery), no details
  - 2.7 yrs mean FU on 65 pts: LR 43%, mets 63%, OS 38.4%, CDFS 12.3%
  - Better prognosis of prominent fibroblastic or MFH-like histologic component

# Literature

- *Bane BL et al, Cancer, 1990* - *MD Anderson CC*

  - 26 pts, 1950-1987, all high-grade lesions
  - Mean age 53.5 yrs, M:F=1.9, 61.5% lower limb
  - Dx: initial biopsy/excision not showing osteoid
  - Mgmt: Surg 9, Surg & Cht 9, Surg & Rxt 3
  - 4.6 yrs FU: LR 50%, mets 61%, NED 27%
  - Size (< 5 cm vs > 5 cm) main prognostic factor

    $p < 0.001$

  - Behaviour more like ST MFH than bone OGS

# Literature

- *Lee JS et al, Cancer, 1995* - *Mayo Clinic*

  - 40 pts, 1915-1988, all high-grade lesions

  - Mean age 50.7 yrs, M:F=1.9, 68% lower limb

  - Management: Surgery 39, Rxt 12, Cht 2

  - LR 45%, mets 65%, 5-yr survival 37%, OS 27%

  - Positive impact of radical/wide margin and chondroblastic subtype

# Literature

- *Ahmad SY et al, J Clin Oncol, 2002* - *MD Anderson CC*

  - 60 pts, 1960-99, AJCC I=3 ,II=25%, III=43%, IV=28%

  - Mean age 55 yrs, M:F=1.6, 52% lower limb

  - Management AJCC<IV: Surgery 35, Rxt 6, Cht 24

    - LR 20%, mets 40%, 5-yr survival 46%

  - 8 month survival if present with mets

  - relatively doxorubicin-resistant, poor-prognosis ST sarcoma that is distinct from OS

# Literature

- *Goldstein-Jackson SY et al, J Cancer Res Clin Oncol, 2005*

  - 17 pts, 17 insts 1986-2002, all high-grade lesions

  - Mean age 44 yrs, M:F=1.7, 47% lower limb

  - Management: Surgery 16, Rxt 1, Cht 16

  - LR 32%, mets 18%, 5-yr survival 77%

  - Positive impact of multi-agent chemotherapy

# Literature

- *Torigoe T et al, J Orthop Science, 2007*

  - 20 pts, 1991-2003, UICC Stage: II=5, III=13, IV=2

  - Mean age 50 yrs, M:F=2.3, 60% lower limb

  - Management: Surgery 19, Rxt 5, Cht 15

  - LR 15%, mets 45%, 5-yr survival 66%

  - Positive impact of chemotherapy – similar findings

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- 48 pts, 1966-2007, 36 admitted, 12 consults
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# Diagnostic Criteria

- Arise in the soft tissue and not be attached to bone/periosteum
- Polyethylene Wear & Hinge Design
- Cemented vs Uncemented Fixation
- Tendon Attachment & Soft Tissue Sealing

# Unsolved & Controversial Issues

- About 1% of all ST sarcomas
- *Wilson H, Ann Surg, 1941*

# Unsolved & Controversial Issues

- Deep Infection and Septic Failure
- Polyethylene Wear & Hinge Design
- Cemented vs Uncemented Fixation
- Tendon Attachment & Soft Tissue Sealing

Musculoskeletal Tumor Advisory Forum
Rizzoli Orthopaedic Institute
Bologna, Italy
August 26, 2009

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