ESPR European Society of Paediatric Radiology
56th Annual Meeting & 42nd Post Graduate Course

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SFCE Société Française de lutte contre les Cancers et les leucémies de l'Enfant et de l'adolescent
RETINOSTOP

Usefulness of MRI as a screening tool to depict head & neck second primary tumors in hereditary retinoblastoma patients formerly treated by external beam radiotherapy: interim report of a national prospective study

institut Curie

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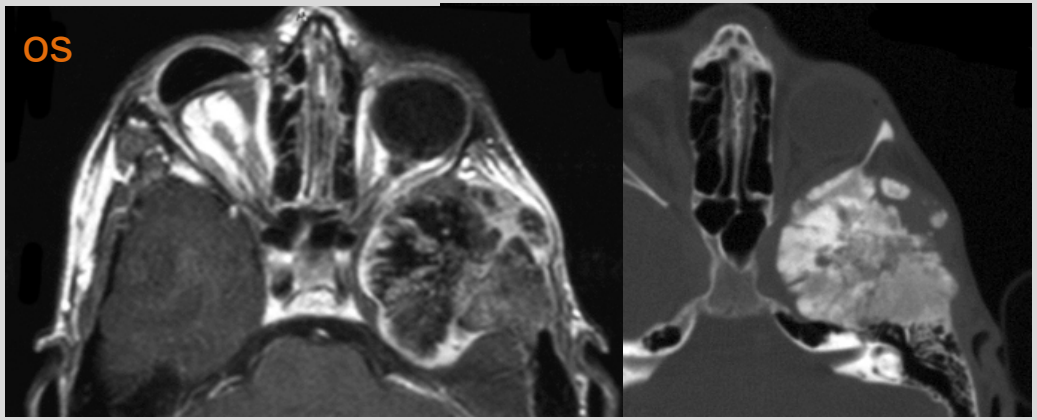
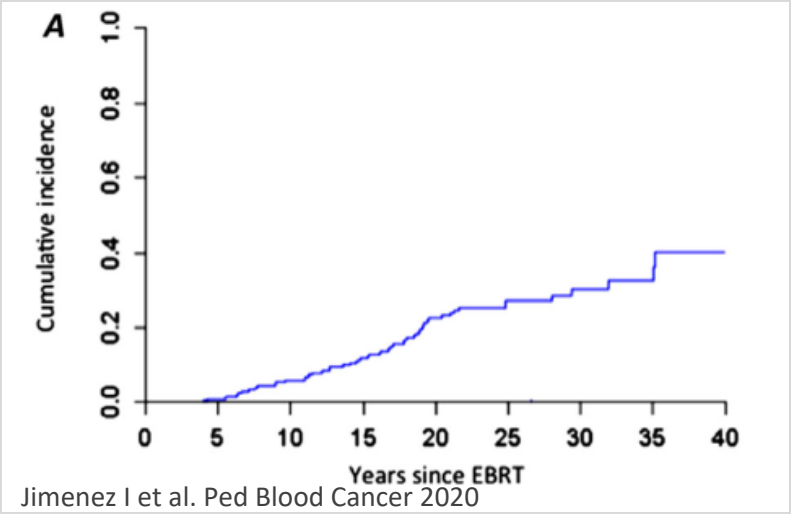
Background

- **Retinoblastoma**
  - Most frequent intraocular neoplasm in children
  - Excellent survival (95%, with optimal management)
  - 40% of patients: germline Rb1 mutation
  - ➢ **Increased risk** of :
    - RB, embryonal midline CNS tumors
    - MSK sarcomas, uterine LMS, cutaneous melanomas
  - EBRT used as conservative treatment until the 90'

- **Second primary tumors (SPT)**
  - *Head & neck* = most frequent location linked to EBRT
  - Life time risk





Jimenez I et al. Ped Blood Cancer 2020

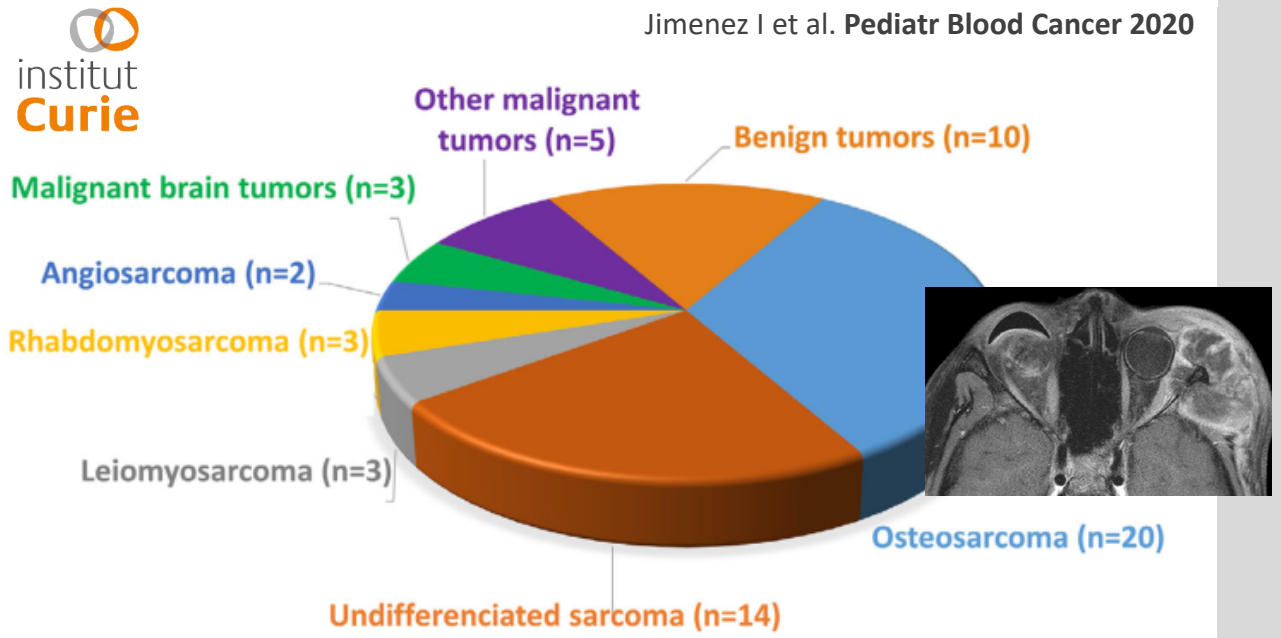
Kleinerman RA, et al. Risk of new cancers after radiotherapy in long-term survivors of retinoblastoma: an extended follow-up**. J Clin Oncol 2005**
Tonorezos ES, et al. Recommendations for Long-Term Follow-up of Adults with Heritable Retinoblastoma. **Ophthalmology 2020**
Jimenez I, Brisse HJ, Aerts I. Craniofacial second primary tumors in patients with germline retinoblastoma previously treated with external beam radiotherapy. **Pediatr Blood Cancer 2020**

Background

	Overall craniofacial primary tumors	Second craniofacial primary tumor	Third craniofacial primary tumor	Fourth craniofacial primary tumor
Tumors (*n*)	60	53	6	1
Median age at diagnosis (y)	18 [5-36]	17.5 [5-36]	21.4 [14.9-25.3]	19.3
Median delay from EBRT (y)	16.9 [4-35]	16.2 [4-35]	20.8 [13.9-24.9]	19.1

Jimenez I et al. **Pediatr Blood Cancer 2020**

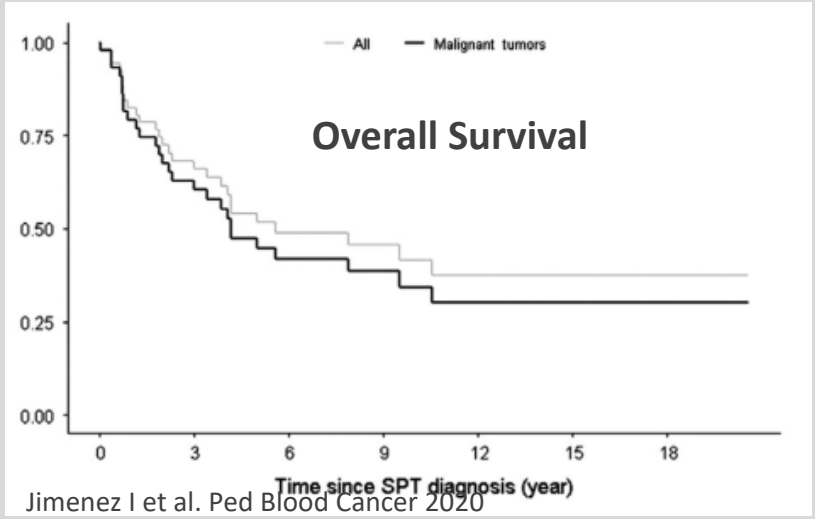
- **Institut Curie experience**
  - 209 patients hereditary RB + EBRT
  - Mean FU: **25 years**
  - **25% patients had SPT**
    - 60 head & neck SPT in 53 patients
    - Median age at SPT diagnosis: 18 y
    - **83% malignant** / 17% benign



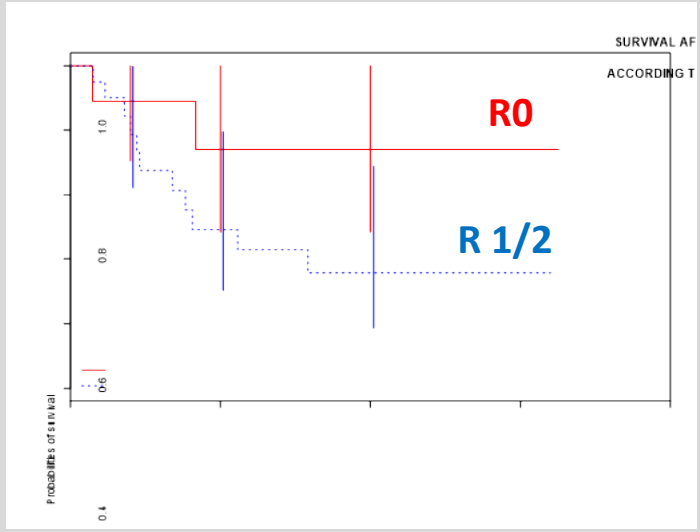
Rodjan F, Graaf P, Brisse HJ, et al. Second cranio-facial malignancies in hereditary retinoblastoma survivors previously treated with radiation therapy: clinic and radiologic characteristics and survival outcomes**. Eur J Cancer 2013**;

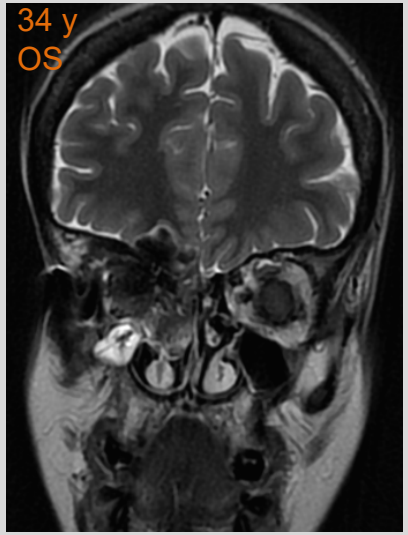
Rational for a screening study

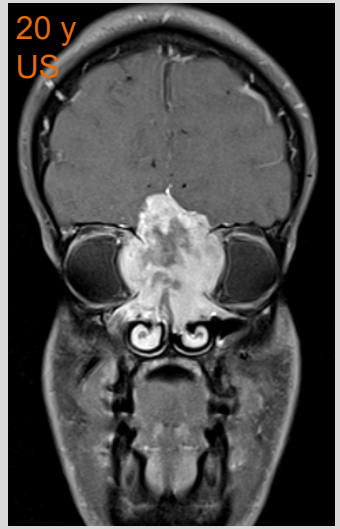
- **Poor prognosis**
  - Low chemosensitivity
  - 15y-OS : 30% (CI: 18-51 %)
  - + residual vision impairement
- **Main prognostic factor**
  - Quality of surgery **R0**
- **Idea**
  - Early depiction / MRI
  - Lower volume: ↗ **R0**
- **Radiological surveillance ?**
  - Currently not supported by evidence *
  - 1 previous series / WBMRI ** (low Se/PPV)
  - But need for prospective evaluation

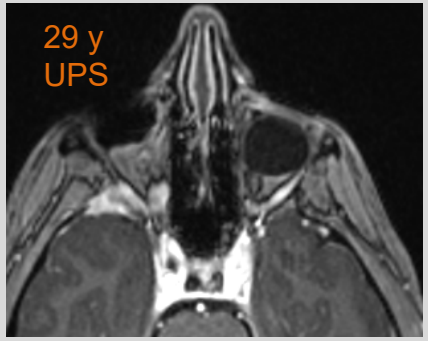


Jimenez I et al. Ped Blood Cancer 2020









* Tonorezos ES et al. **Ophthalmology 2020**

Friedman DN et al. Pediatr Blood Cancer 2014**

DepISCARRH Study description & patients

- **Study profile**
  - IRB-approuved non-randomized Interventional **prospective national** multicentric study
  - Promotion: Institut Curie ; financial support / Ligue contre le Cancer ; SFCE Label
  - ClinicalTrial.gov: NCT03026998
  - Study duration: 10 years (2017 – 2027)

- **Eligibility**
  - **Inclusion criteria**
    - Hereditary RB (i.e., bilateral, multifocal, familial, identified RB1germline mutation, 13q deletion)
    - RB treatment including EBRT
    - Delay from EBRT termination > 5 years
    - Age at inclusion ≥ 7 y
  - **Non-inclusion criteria**
    - Already treated for head & neck second primary sarcoma
    - Contraindication for MRI

Methods

- **Patients information**
  - Mailing: information about the study to all patients cohort
  - Presentation during RB patients parents' association
  - Social media, website
  - Consultation with pediatricians / ophthalmologists + informed consent

- **MRI once a year**
  - Specific guidelines: **face/brain**
    - **T1** (sag+axial), **FS-T2 or STIR** (ax+cor), ax **FLAIR**, **DWI**, *No Gd* (unless suspicious lesion)
  - DICOM data centralisation

- **Central radiology review**
  - Systematic review by one senior radiologist *(the one who speaks)*
  - Review report sent to patients and referent physician
  - Second MRI if necessary

Results

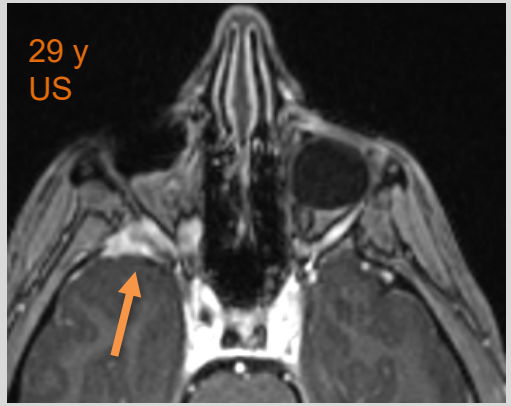
- **Interim report after 5 years**

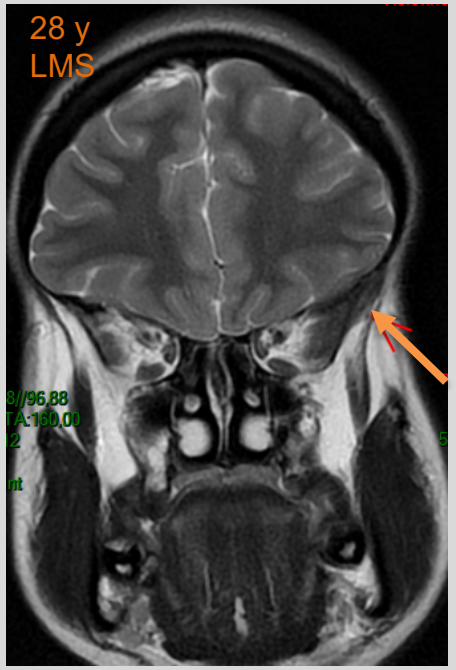
  - 03/2017 – 03/2022
  - Theoretical patients file: n=173
  - Inclusions: n=76
  - Mean age at inclusion: 20 y (range: 7-42 y)
  - 161 MR examinations reviewed

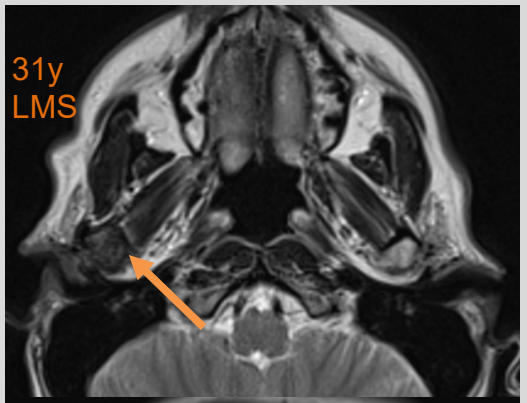
Results – Malignant SPT

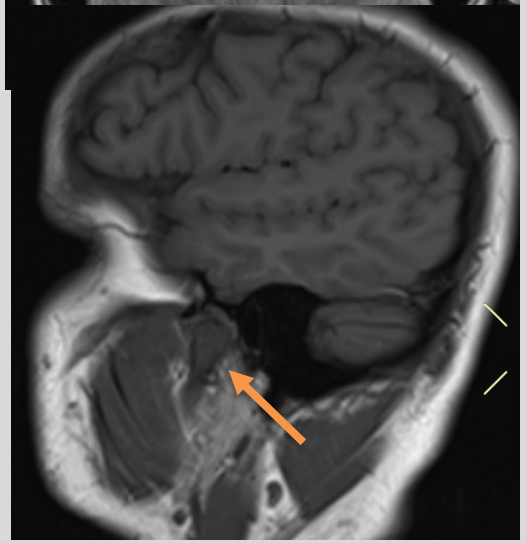
- **No malignant SPT MR depiction**

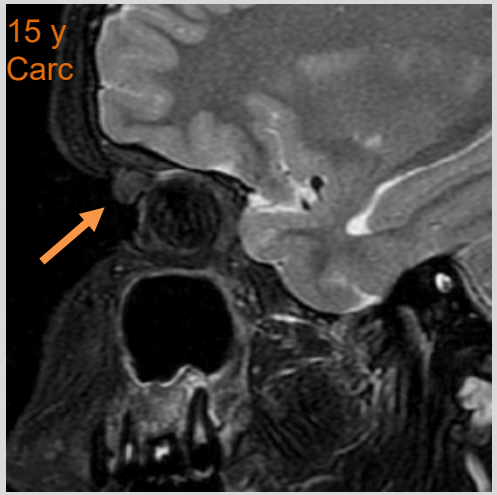
- **Symptomatic patients: n=5**
  - Symptoms *before inclusion*
    - 3 facial bones sarcomas
    - 2 palpebral carcinomas





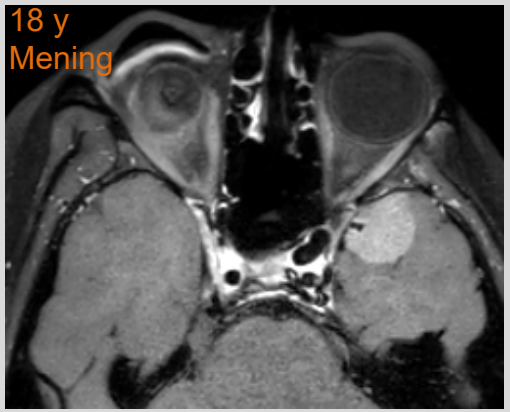


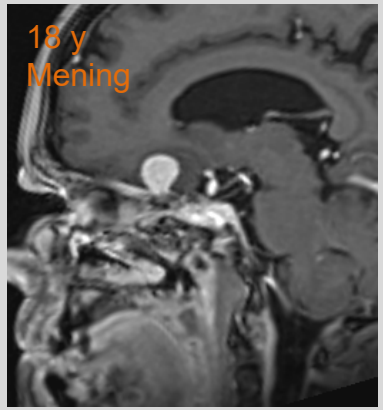


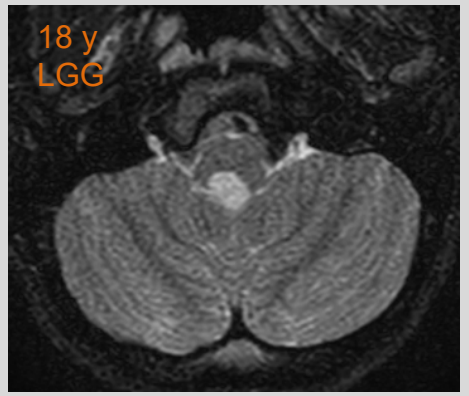


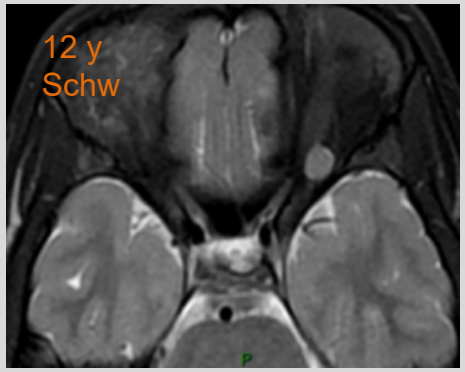
Results – Benign SPT

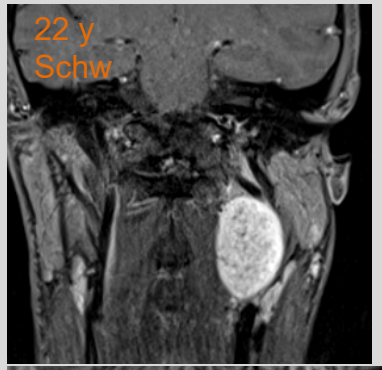
- **Benign tumors MR depiction**
  - **n=16**/76 (21%) patients
  - Variable conditions
    - 5 meningiomas
    - 2 CNS low-grade tumors (4th V)
    - 3 schwannomas
    - 4 benign bony lesions (stable / FU)
    - 1 pharyngeal fibrous polyp
    - 1 orbital inclusion cyst

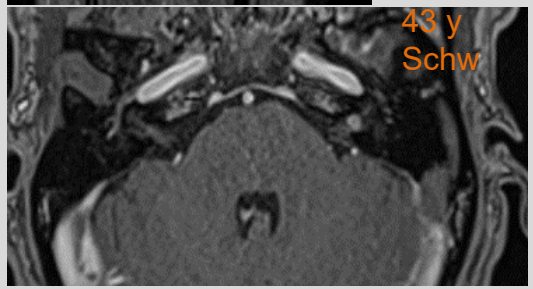












- **Local treatment required in 6/16 (37.5%)** patients
  - Meningiomas Surgery 1, RT 2, 2 stop progesterone agonist
  - Schwannomas Surgery 2
  - Growing LGG Surgery 1
  - Phar. polyp Surgery 1

Discussion / Conclusion

- **MR Screening for hereditary RB patients after EBRT**
  - ✓ Unique prospective trial / high risk population
  - ✓ Limitation: Inclusion rate low (long survivors)

- **Preliminary data**
  - Still no evidence of usefulness for *malignant* SPT depiction
  - High rate of benign tumors/conditions (> 20%)
  - 1/3 of benign lesions required local treatment (**meningiomas, *schwannomas***)
    - ➢ *Alternative benefit from screening ?*

- **Meanwhile, patients' education is mandatory** (early symptoms)
  - Early symptoms (persistent sinusitis, pain, bump)
  - Progesterone agonist treatments must be avoided / women