

Children with LFS

Cancer
predisposition
surveillance clinic

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George Pantziarka TP53 Trust



Cancer predisposition – choices we make



Above

the line
thinking + behaviours



Hope

See it

Make choices

See possibilities

Own it

Solve

seek solutions

Accountable

Find better ways

Take responsibility

seek + provide
Feedback

Take action

Make
a
Choice!

Things happen
but it is your
response that
determines if
the outcome is
ultimately ^{positive} or ^{negative}

Below

the line
thinking + behaviours

Ignore
Deny

Stay
stuck

Blame

Deny

Excuses

Gossip

Do nothing

Victim

See problems
obstacles

Wait for others

Find fault

Block

No control

see
failure

Event
+ your
response



outcome

positive
???

negative
???

Li Fraumeni Syndrome

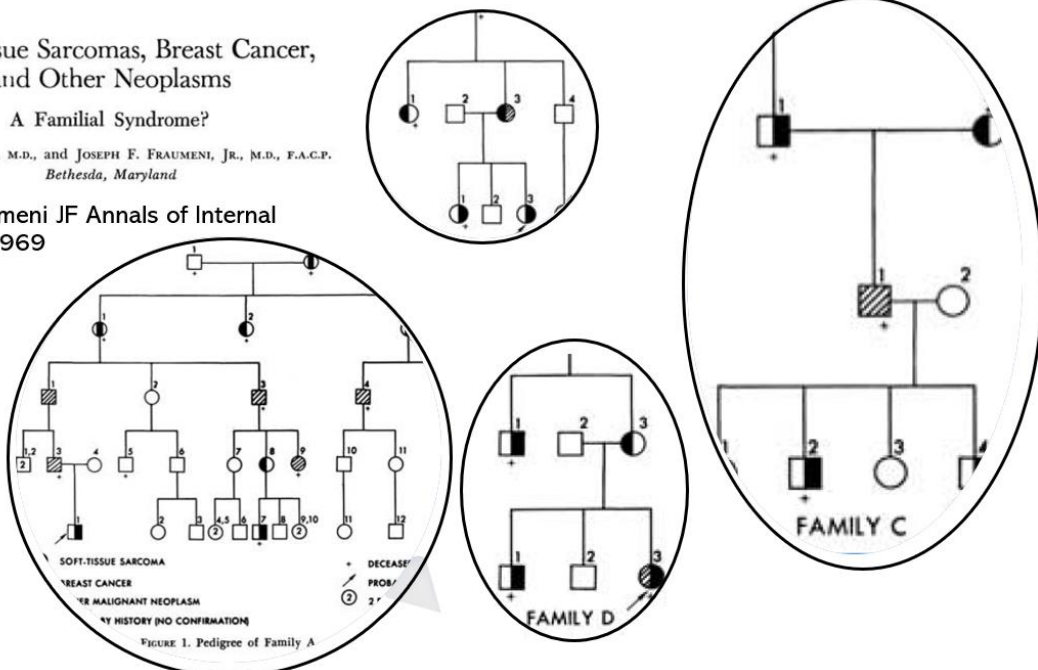
- In 1969 Fredrick Li and Joseph Fraumeni described four families from studies of childhood rhabdomyosarcoma "A Familial Syndrome"
- Observed that the families had striking histories of sarcoma and other early onset cancers
- Tumour banking



Tumour banking

Soft-Tissue Sarcomas, Breast Cancer, and Other Neoplasms
A Familial Syndrome?
FREDERICK P. LI, M.D., and JOSEPH F. FRAUMENI, JR., M.D., F.A.C.P.
Bethesda, Maryland

Li FP, Fraumeni JF Annals of Internal medicine 1969



Biochemical and imaging surveillance in germline TP53 mutation carriers with Li-Fraumeni syndrome: 11 year follow-up of a prospective observational study



Anita Villani, Ari Shore, Jonathan D Wasserman, Derek Stephens, Raymond H Kim, Harriet Druker, Bailey Gallinger, Anne Naumer, Wendy Kohlmann, Ana Novokmet, Uri Tabori, Marta Tijerin, Mary-Louise C Greer, Jonathan L Finlay, Joshua D Schiffman, David Malkin

CCR PEDIATRIC ONCOLOGY SERIES

Cancer Screening Recommendations for Individuals with Li-Fraumeni Syndrome



Christian P. Kratz¹, Maria Isabel Achatz², Laurence Brugières³, Thierry Frebourg⁴, Judy E. Garber⁵, Mary-Louise C. Greer⁶, Jordan R. Hansford^{7,8}, Katherine A. Janeway⁹, Wendy K. Kohlmann¹⁰, Rose McGee¹¹, Charles G. Mullighan¹², Kenan Onel¹³, Kristian W. Pajtler^{14,15}, Stefan M. Pfister^{14,15}, Sharon A. Savage², Joshua D. Schiffman¹⁶, Katherine A. Schneider⁵, Louise C. Strong¹⁷, D. Gareth R. Evans¹⁸, Jonathan D. Wasserman¹⁹, Anita Villani²⁰, and David Malkin²⁰



The NEW ENGLAND JOURNAL of MEDICINE

Germline mutation in predisposition genes in paediatric cancer patients

Zhang, Walsh, Wu et al 2015
New England Journal of Medicine

nature

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nature > articles > article

Open Access | Published: 28 February 2018

The landscape of genomic alterations across childhood cancers

Susanne N. Gröbner, Barbara C. Worst, Joachim Weischenfeldt, Ivo Buchhalter, Kertine Kleinheinz, Vasilisa

8-10 % Children with cancer found to have CPS
4% TP53 / LFS
40% family history of cancer

The role of Cancer Predisposition in childhood cancer

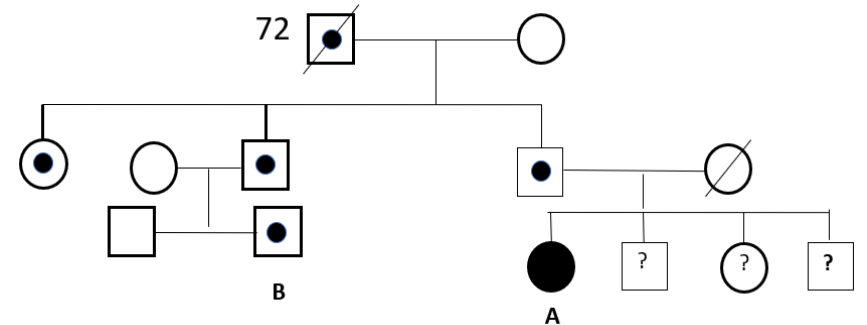
Childhood cancer is rare (1%)

4200 children and TYA diagnosed with cancer each year in the UK

- Cancer predisposition (10%) 420 children & TYA /year
- TP53 (4%) 200 patients expected/year

Changes in medical practice:

- WGS for all children with new cancer diagnosis



- The generation study (neonatal WGS)
- Young mothers with breast cancer

Who do we test and when?

Testing in childhood – important?

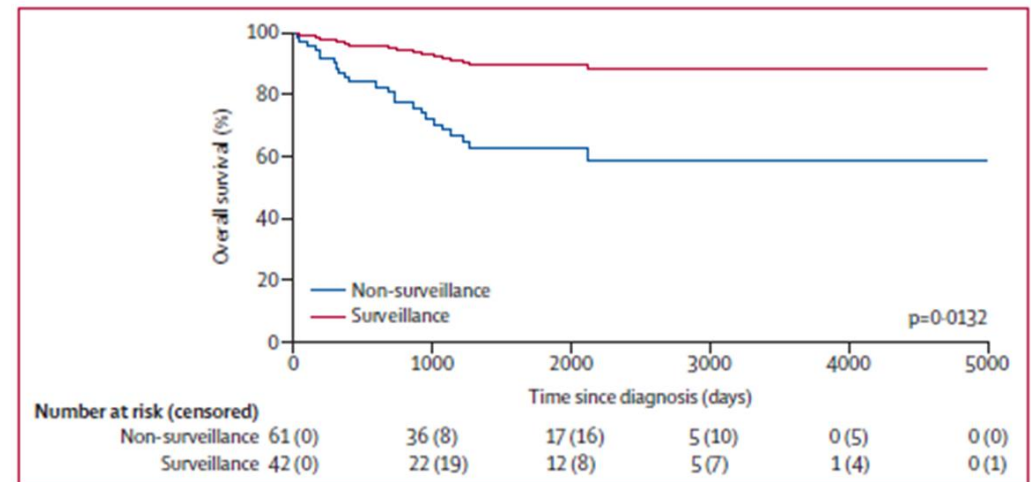
A significant number of cancers at a young age;

- 41% by 18 years of age
- 22% diagnosed < 5 years of age
- 4% diagnosed < 1 year of age

Bougeard et al JCO 2015

Surveillance -

- David Malkin's group (Villani et al)
- 27 children
 - 21 non-surveillance (4 crossed over)
 - 6+4 surveillance
 - Non-surveillance (Deceased 52%)
 - Surveillance (Deceased 33%)



Funding, referrals and numbers

Historical

- Joint clinic with genetics
- Alternate months 1-2 patients

Current

- 2-3 clinics/month
- 2 consultants / 1 CNS / 1 research nurse
- **Needed: psychology support (families)**

- 117 children (TYA) registered
- 80 children currently on surveillance

- Age Average 10.8yrs (6 months – 20)
- 52% female

Surveillance (LFS)

- Yearly whole body and head MRI
 - Awake / sedation / General anaesthetic
- 4-6 monthly Abdominal USS
- Clinical examination
- No biochemical markers (blood or urine)
- Red Flag Symptoms
 - Headache
 - Nausea
 - Vomiting
 - Seizure
 - Abnormal eye movement / vision
 - Lumps and bumps
 - Bruising
 - Pain (growing pain)

Entry into the clinic

(N=117)

Children presenting with cancer

N = 36

7 died of primary cancer (20%)
1 died of 2nd malignancy
(non-surveillance) 22%

28 cross-over
to surveillance

Cancer

2nd / 3rd malignancy
N = 11 (39%)
↳ 2 died

metastatic
progression of
primary cancer
n = 3

Extended
anatomical site
surveillance

↳ ALIVE

Unaffected carriers

N = 61

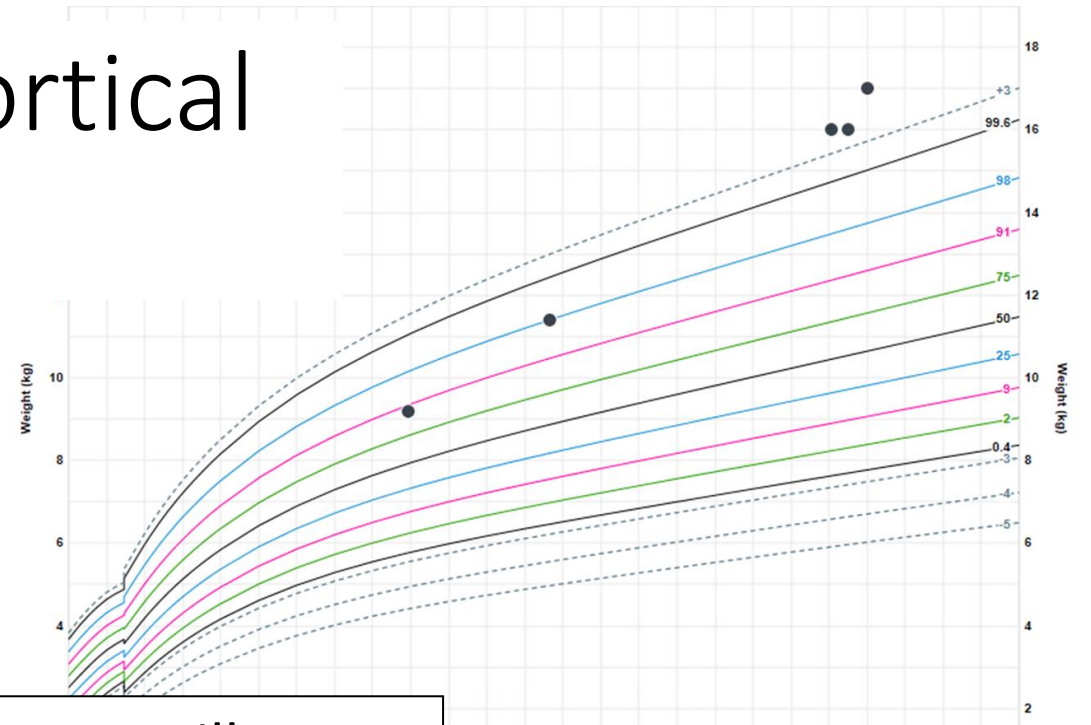
Predictive testing
(family history)

SURVEILLANCE

False +ve

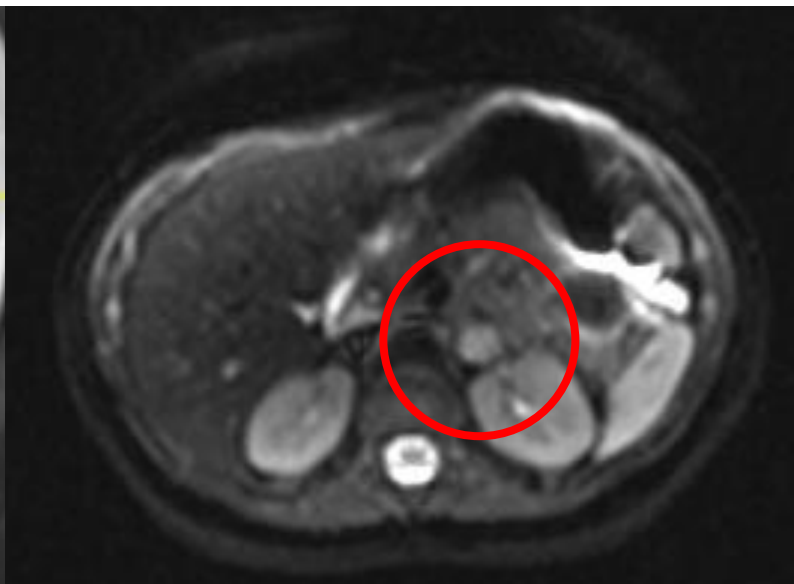
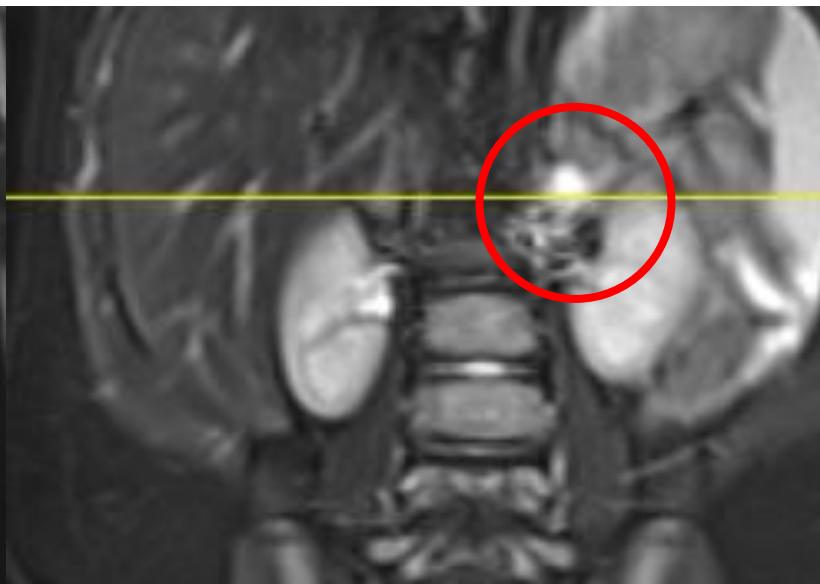
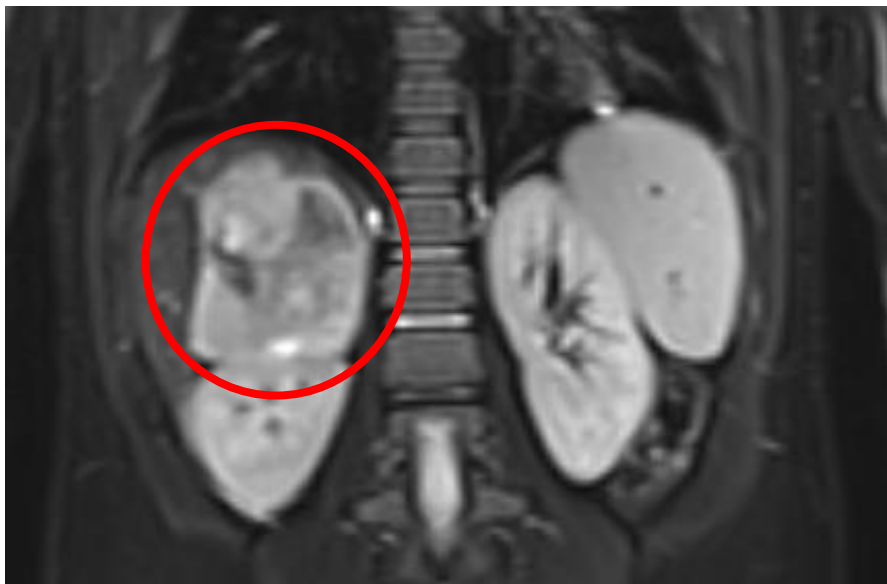
3 Cancer
(1 multiple
→ died)

Early diagnosis of Adrenocortical carcinoma

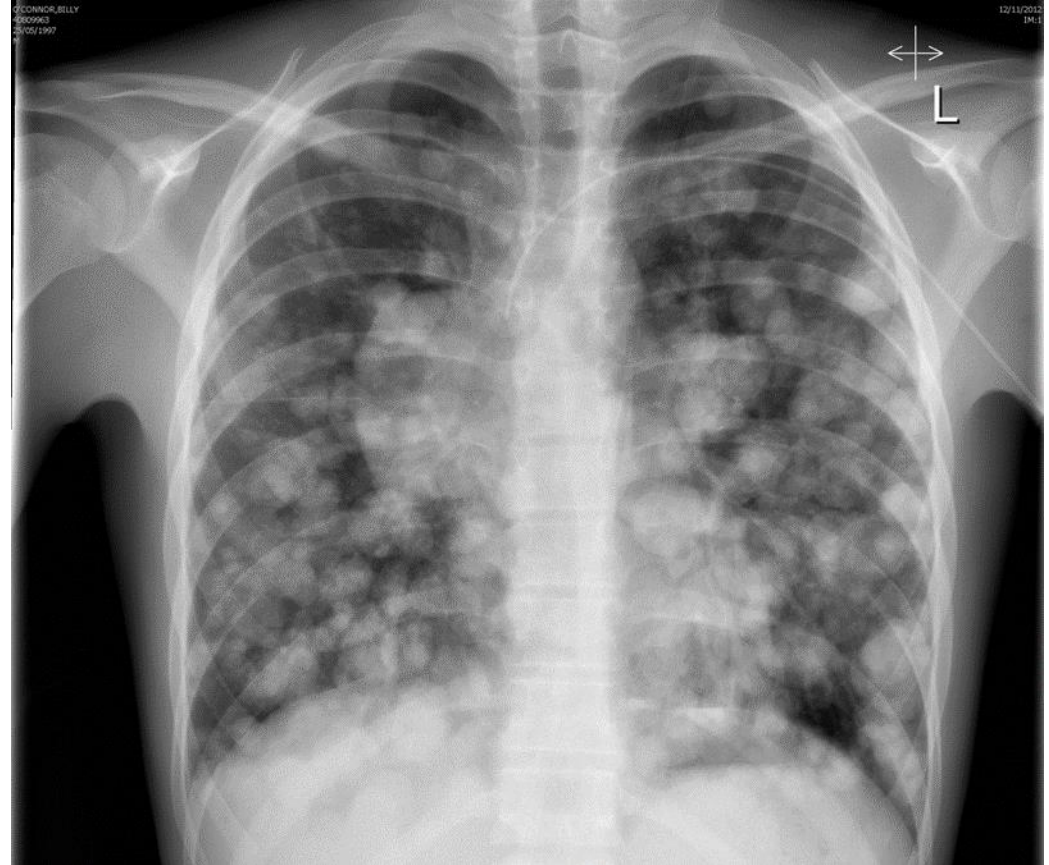
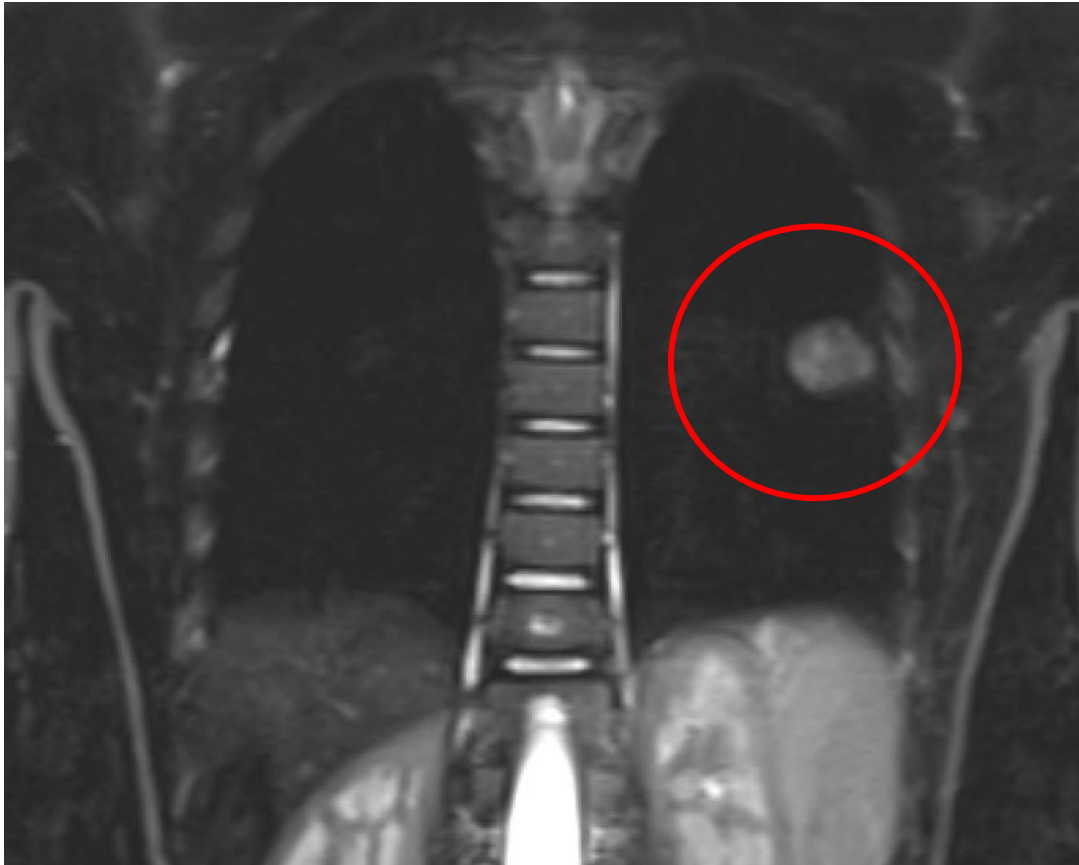


3-year old boy - delayed diagnosis

Sister (20m) on surveillance



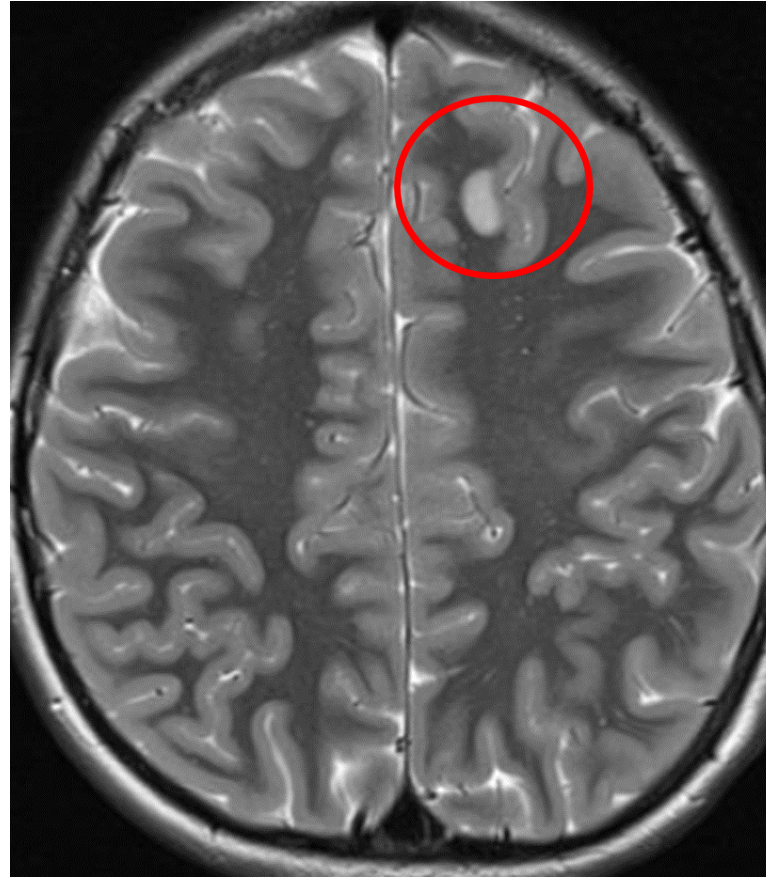
TP53 Surveillance (early diagnosis or recurrence)



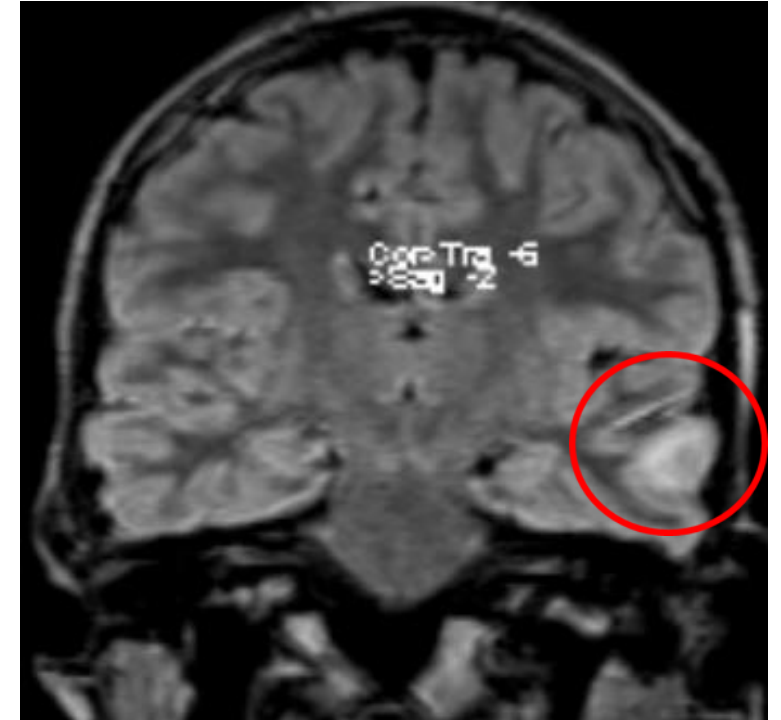
CNS lesions on surveillance – changing outcome?



14-year old Grade II Astrocytoma /
LGG glioma – surgery only.



11-year old (normal tissue)

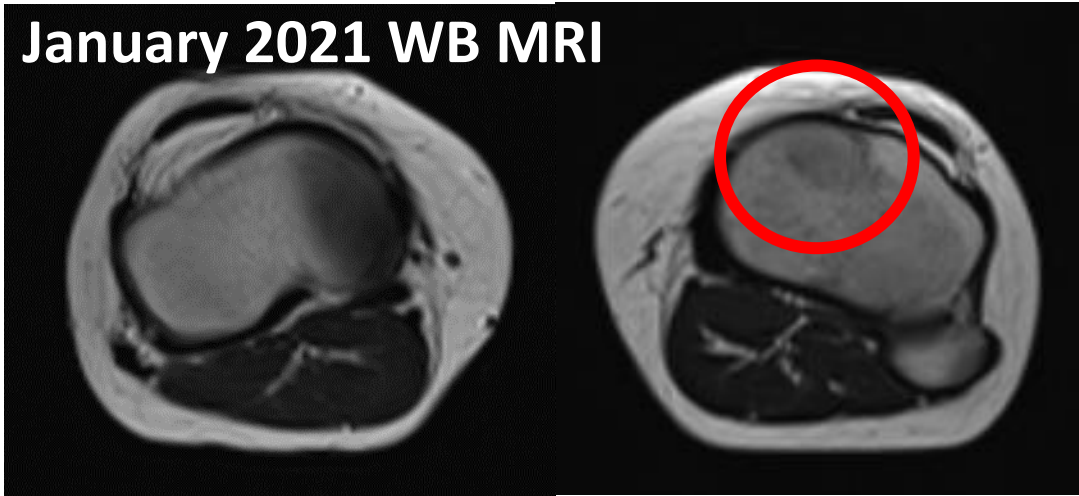


12-year old – no abnormal
tissue on pathology

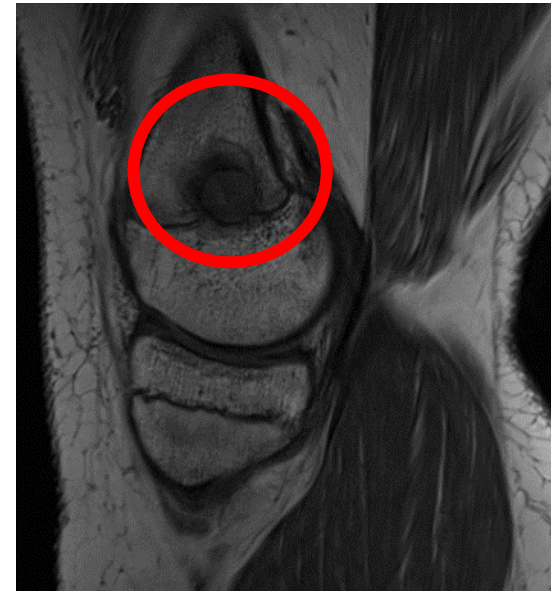
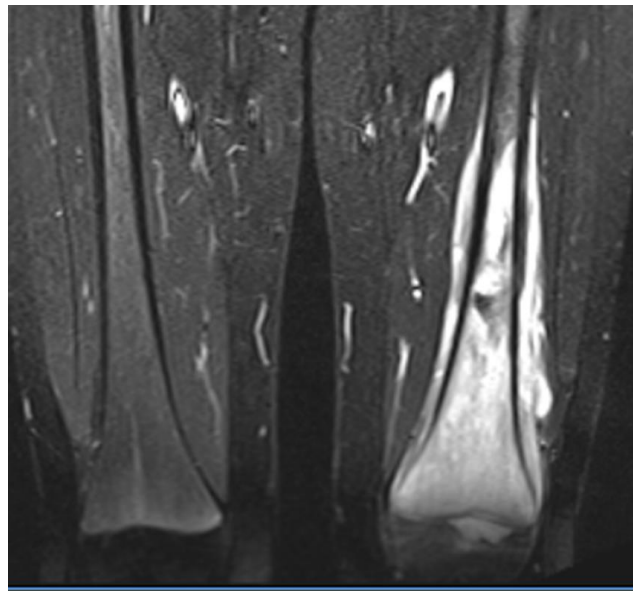
Challenges of WB MRI

False negative

False positive



January 2022
WB MRI



Questions and challenges

Surveillance

- Does it make a difference?
 - Yes, on individual level
 - Uncertain if impact on outcome
 - Too early – few cancers in surveillance group
 - Are we changing risk but resection of benign (CNS) tumours? / impact on risk of metastatic disease with early diagnosis? / early mastectomy?
- Collaborations and development of surveillance in the UK?
 - SIGNIFY study (adults)
 - MILI study (>16)
 - Research and collaborations
- MILI study for children????

Thank you

Dr Karin Straathof

Ms Helen Speight (CNS)

Ms Leanne Smith (research nurse)

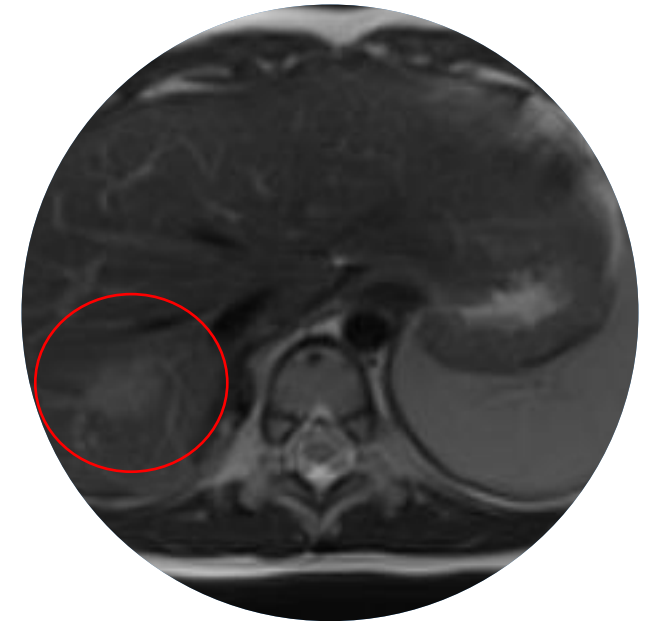
Dr Naomi Stageman (SpR)

Dr Raheleh Rahbari (Sanger)


The children and families in clinic



Questions?



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NHS Foundation Trust