



MY STORY FROM GERMANY

LFS UK 2019
7th September 2019



CV - CONFLICT OF INTEREST



10 years medical doctor

6 years clinical research,
mainly breast cancer

Breast cancers, LFS

Patient advocate

ePAG representative for Li Fraumeni
syndrome for ERN GENTURIS

Dr. Rita Magenheim drcancergirl
FUCK CANCER !

BREAST CANCER SCREENING

- Breast cancer screening start: **Germany: 50 years**
UK: 45 years
USA: 40 years low risk, high risk earlier
 - Breast **cancer risks assesment** never done
 1. Family history: mother 3 primary cancers (37y cervix, 48y lung, 63y pancreas)
 2. Eastern European (Ashkenazi) Jewish ancestry
 3. Normal weight
 4. Over 15 years night shift
 5. Child birth 38 and 40 years
 - Mammography: neg
Ultrasound 4 and 7 mm lesion in both breast
Breast MRI left negativ
- „ no breast or ovarian cancer = Family history: empty“**

BREAST CANCER TREATMENT

- Invasive breast cancer left, DCIS right (probably cancer as well)
- PEN II Risk Model: 40 % for BRCA1 and 2 mutation
- Recommendation: Lumpectomy, irradiation

Genetic counselling: Fast track result in 2-3 months...

- Genetic test in Hungary in 10 days
- Li Fraumeni diagnosis
- Bilateral mastectomy
immediate reconstruction
over the muscle silicone implant

Patients are not correctly informed about all the possible options..

EVIDENCE-BASED vs. PERSONALIZED MEDICINE



Evidence-based medicine

Doctors **think OR know** what the best treatment is

Personalized medicine

The best treatment **for the majority OR for you**

PERSONALISED TREATMENT DECISIONS

- **When to start with the therapy**

Neoadjuvant hormonal therapy (before the surgery)

- **Surgery planning**

Bilateral sentinel lymph node removal (right only DCIS)

Should be considered during PROPHYLACTIC MASTECTOMY as well

- **Additional examination on the tumor tissue**

HER-3 measurement

Dual HER-2 blockade (trastuzumab + pertuzumab)

- **Therapeutic drug monitoring**

Tamoxifen metabolite serum level measurement, 40 mg dosage (CYP2D6)

- **Steroid before chemotherapy**

8 mg Dexamethasone before all vs. only before the first 3 administration of paclitaxel



This is
not a
whole
body!

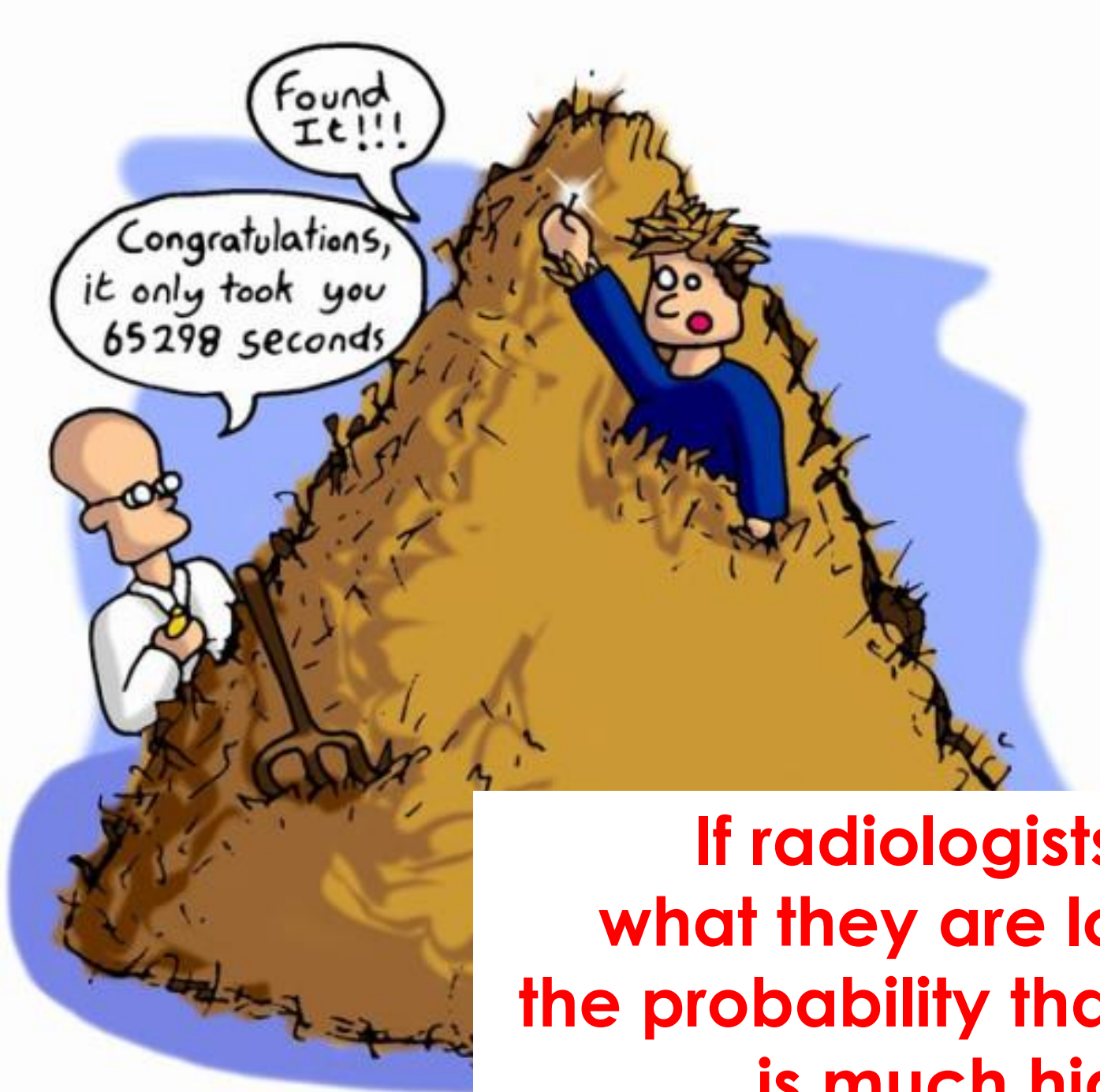
WHOLE BODY MRI IN GERMANY

PROBLEMS

- Mostly **unknown** diagnostic method
- **3 month waiting time** for kids
- **In narkosis** until the age of 6-9
No preparation programm
No TV in the MRI
- Siblings on one day not possible
- Radiologists have limited clinical information

SOLUTION

- Only in LFS centers
- Training for the radiologist
- Preparation course for the kids
- LFS specific questionnaire



**If radiologists know
what they are looking for
the probability that they find it
is much higher.**

ADRENAL GLAND AND ABDOMINAL ULTRASOUND



I see with sound



What's your superpower?

1. „It is impossible to examine adrenal gland with abdominal ultrasound“
2. „It is very difficult“
3. „Of course I can“

Ultrasound experts,
for children and adults,
whole family.





PERSONALIZED SCREENING PROTOCOL

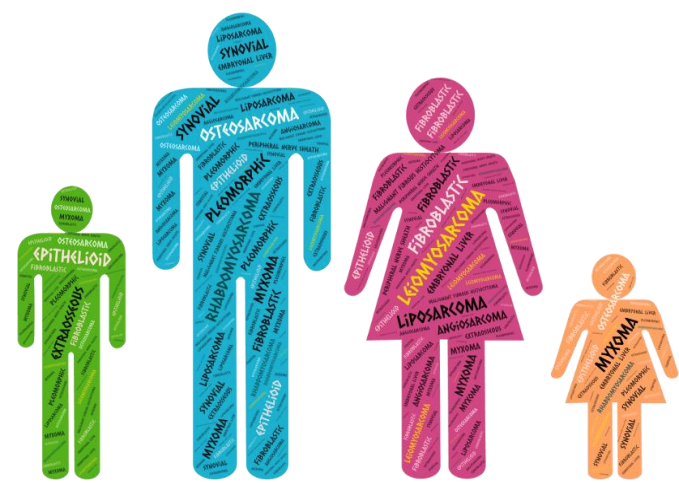
- **Family history**
- **Personal history** (IVF and ovarian cancer risk)
- **Treatment** (tamoxifen endometrium cancer)
- **Genotype – phenotype correlation**
- **Most common tumors** for gender and age (Registry...)

Some guidance in the guideline would help:

If.... consider adding to the screening protocol

PERSONALIZED SCREENING PROTOCOL

Cancer	Additional risk factor	Additional examinations
Ovarian	Endometriosis 3 x IVF	Adnexectomy Vaginal ultrasound and tumor marker (CA125)
Endometrium	Tamoxifen	Hysterectomy Vaginal ultrasound until the surgery
Lung	Mother 48 y	Tumor marker (CEA, CYFRA 21-1) every 6 month
Pancreatic	Mother 63 y	Tumor marker (CEA, CA 19-9)
Adrenocortical	2 published cases genotype-phenotype	Abdominal ultrasound every 6 month for me every 3 months for my sons
Skin	Dysplastic naevus	Dermatologist every 6 month Tumormarker (S100)
Colorectal		Septin-9 test between the colonoscopies



MOST COMMON TUMORS FOR **ADULT** WITH LFS

Males

1. Soft tissue
2. Brain
- 3. Colorectal/Gastrointestinal**
4. Bone
5. Skin
6. Lung
7. Hemopoetic
8. Prostate

Females

1. Breast
2. Soft tissue
3. Brain
- 4. Gastrointestinal**
5. Lung
6. Ovary
7. Skin
8. Bone

CANCER TREATMENT OPTIONS

HORMONE
THERAPY



SURGERY



BONE MARROW
TRANSPLANTATION



CHEMOTHERAPY



TARGETED
THERAPY



IMMUNOTHERAPY



RADIATION
THERAPY



PSYCHOTHERAPY



NUTRITION THERAPY



CANCER TREATMENT OPTIONS

IMMUNOTHERAPY



RADIATION THERAPY



TARGETED THERAPY



CHEMOTHERAPY



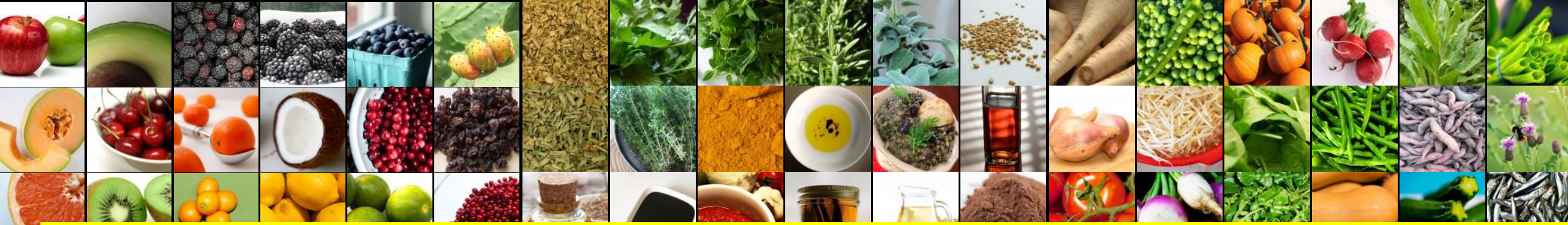
BONE MARROW TRANSPLANTATION

SURGERY



HORMONE THERAPY





Proven anticancer effect



<https://www.eattobeat.org/>
The Angiogenesis Foundation

NUTRITION THERAPY

- What to eat
- When to eat „Intervall fasting“
- Weight

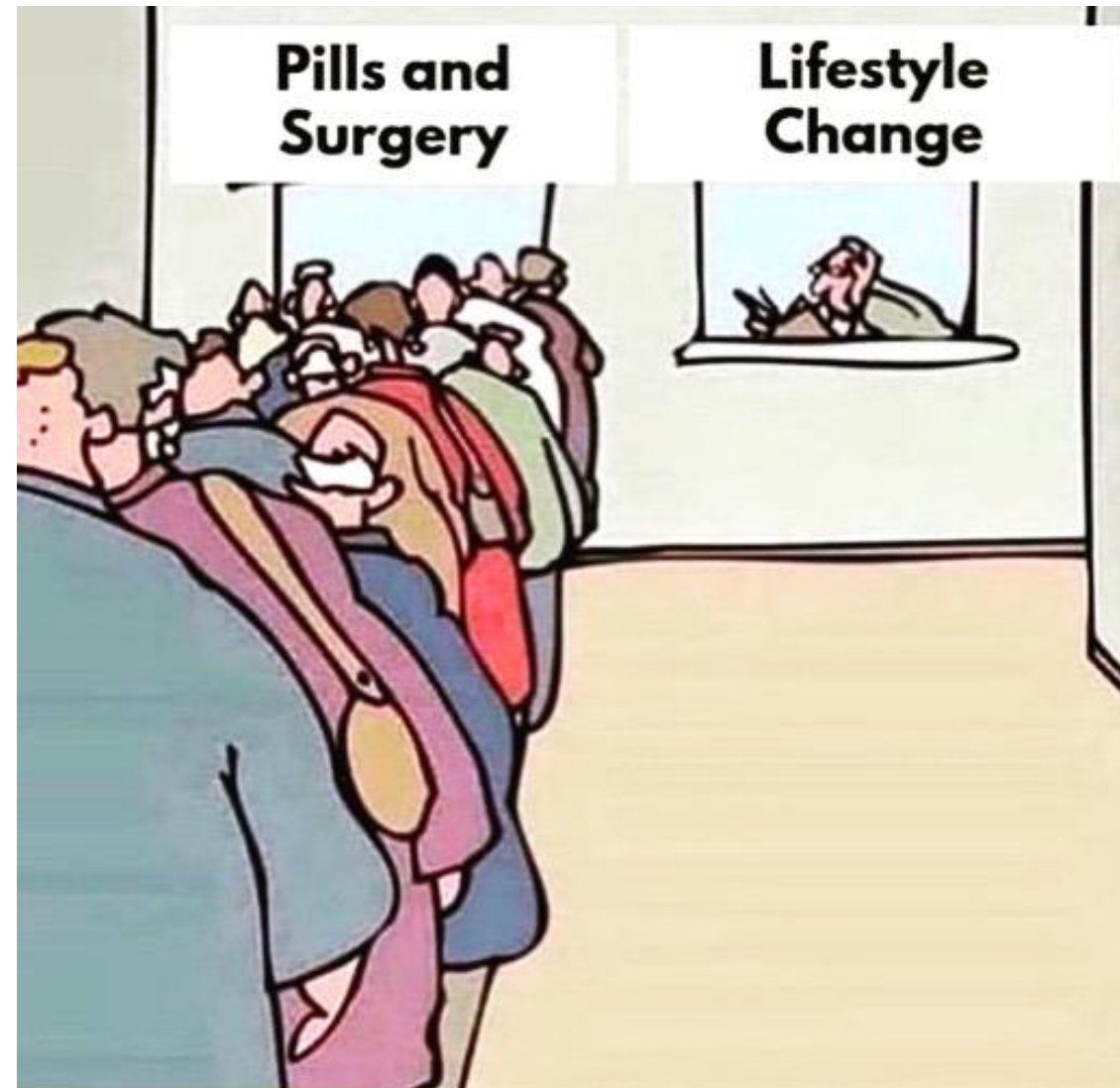
Nutriceutica:

- Nigella sativa (Black seed oil)
- Fermented wheat germ extract (Avemar)



CHEMOPREVENTION

- **Tamoxifen** reduces breast cancer risk by 33% !
Not only 20 mg dose exist...
- Off-label:
 - Metformin**
 - Propranolol**
 - Aspirin**



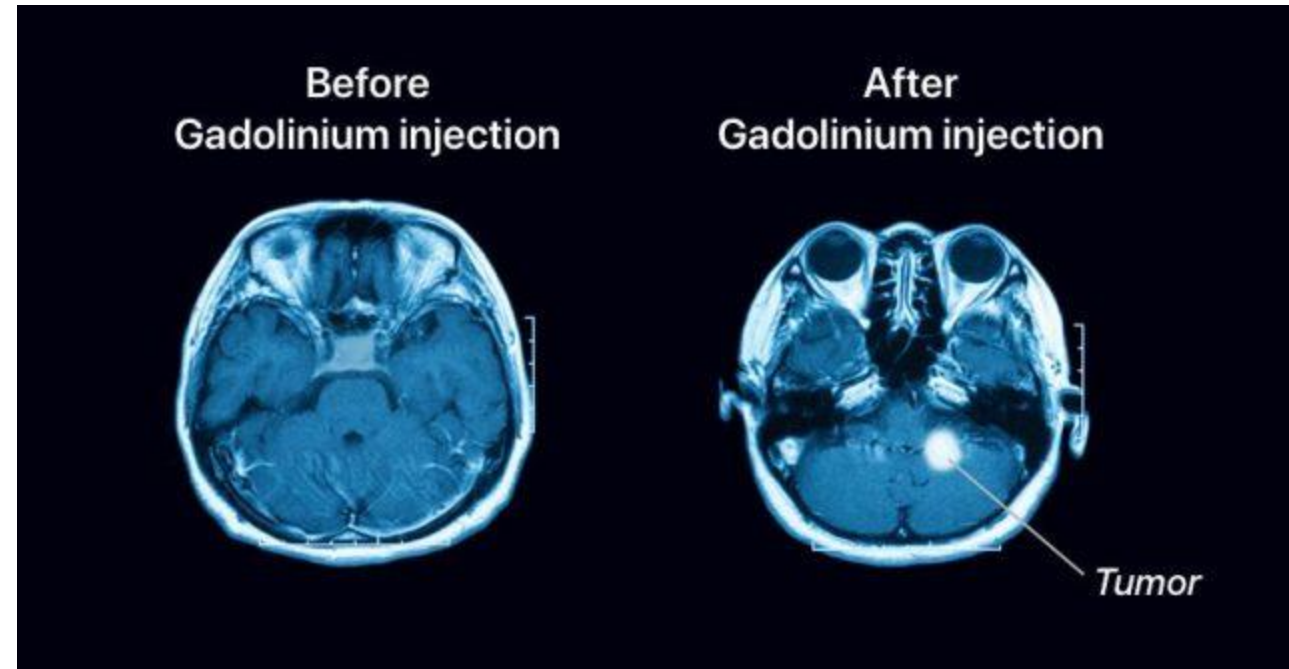
GADOLINIUM

If surveillance includes brain MRI, at least the first scan **should** be conducted using dedicated brain MRI with Gadolinium enhancement.

Breast MRI should always be conducted with gadolinium contrast agent.

Linear vs. macrocyclic

Gadolinium Pass



Goals: Raise awareness
Inform patients
Build a network
Promote research

LI-FRAUMENI ASSOCIATION - GERMANY

- Germany: inhabitants 80 million
Estimated number of LFS patients: **16.000**
Diagnosed LFS patients: estimated 200-300 **1-2 %**
- Very limited number of LFS experts and LFS centers
- **LFS register**: 30 patients
Open for other countries
<http://www.krebs-praedisposition.de/en/>

Maßnahmen zur Früherkennung von Krebserkrankungen

Für alle Personen mit LFS, beginnend ab klinischer oder genetischer Diagnosestellung, lebenslang
(Clin Cancer Res; 23(11): e38-45)

Kinder (Geburt bis 18 Jahre)	Erwachsene
<ul style="list-style-type: none"> Körperliche Untersuchung alle 3-4 Monate Zeitnahe ärztliche Untersuchung bei medizinischen Problemen Ultraschall Bauch und Becken alle 3-4 Monate Falls Ultraschall Bildqualität unzuverlässig: Tumormarker im Blut Jährlich MRT vom Kopf Jährlich Ganzkörper MRT 	<ul style="list-style-type: none"> Körperliche Untersuchung alle 6 Monate Zeitnahe ärztliche Untersuchung bei medizinischen Problemen Jährlich MRT vom Kopf Jährlich Ganzkörper MRT¹ Jährlich Ultraschall Bauch und Becken Untersuchung des Magendarmtraktes alle 2-5 Jahre ab 25. Lebensjahr Jährlich hautärztliche Untersuchung <p><i>Zusätzlich für Frauen</i></p> <ul style="list-style-type: none"> Risikobewusstsein für Brustkrebs für Frauen Klinische Brustuntersuchung zweimal jährlich ab 20. Lebensjahr Jährliches Brust-MRT-Screening (von 20-75 Jahre)¹ <p>¹Die Brust-MRT sowie Ultraschalluntersuchung der Bauchorgane und des Beckens sollte sich mit der jährlichen Ganzkörper MRT abwechseln (mindestens ein Scan alle 6 Monate)</p>

Früherkennungsempfehlungen

Für alle Personen mit LFS, beginnend ab klinischer oder genetischer Diagnosestellung, lebenslang
(Clin Cancer Res; 23(11): e38-45; Details: <http://clincancerres.aacrjournals.org/content/23/11/e38>)

Kinder (Geburt bis 18 Jahre)	Erwachsene
<ul style="list-style-type: none"> Körperliche Untersuchung alle 3-4 Monate, einschließlich Blutdruckmessung, Wachstumskurve und neurologischer Status Sofortige Abklärung neuer Symptome US Abdomen+Becken alle 3-4 Monate Im Falle unzureichender US Qualität: Alle 3-4 Monate: Blutentnahme (Gesamt-Testosteron, Dehydroepiandrosteronsulfat und Androstendion) Jährlich MRT-Schädel (zunächst mit Kontrast, danach ohne Kontrast, wenn vorherige MRT normal und keine neuen Aspekte) Jährlich Ganzkörper MRT 	<ul style="list-style-type: none"> Körperliche Untersuchung alle 6 Monate Sofortige Abklärung neuer Symptome Ganzkörper-MRT¹: Kopf bis Fuß, einschließlich Extremitäten Jährlich MRT-Schädel (zunächst mit Kontrast, danach ohne Kontrast, wenn vorherige MRT normal und keine neuen Aspekte) US Abdomen+Becken alle 12 Monate¹ Obere Endoskopie und Koloskopie alle 2-5 Jahre (ab 25 Jahre) Jährliche dermatologische Untersuchung <p><i>Zusätzlich für Frauen</i></p> <ul style="list-style-type: none"> Brustkrebs-Risikobewusstsein Klinische Brustuntersuchung zweimal jährlich (ab 20 Jahre) Jährliches Brust-MRT (20-75 Jahre)¹ Risikominimierende bilaterale Mastektomie erwägen <p>¹Brust MRT/ US Abdomen+Becken mit jährlicher Ganzkörper MRT abwechseln (mindestens ein Scan alle 6 Monate)</p>

ZWEITES DEUTSCHES LI-FRAUMENI-SYNDROM-FAMILIENTREFFEN

14. UND 15. SEPTEMBER 2019, HANNOVER



2nd German Li-Fraumeni family meeting



THANK YOU!

Anticancer lifestyle