SUPPLEMENT

Baseline Surveillance in Li-Fraumeni Syndrome using whole body magnetic resonance imaging: A Meta-Analysis

TABLE OF CONTENTS

Table 1: Cohort details

Title	Institution(s)	Country	Trial registration	No. of partic	Eligible age range (yrs)	Eligibility criteria
NCI LFS Study (NCI LFS)[1] (JAMA Onc in press) 2011- ongoing	National Cancer Institute	USA	ClinicalTrials.gov; NCT01443468	116	>3 to 100	• Known *TP53* mutation carrier and >6 months from chemotherapy or radiation therapy or after recovery from a curative cancer surgery
Evaluation of Rapid Whole-Body Magnetic Resonance Imaging in the detection of tumors in Li-Fraumeni syndrome carriers (ACCCC) 2012 - ongoing	AC Camargo Cancer Center	Brazil	IRB: ACCCC 1832/13 ; CAAE 21030413.4.0000.5432	68	All ages	• Known *TP53* mutation carrier
Screening with Whole Body MRI in Patients with Li-Fraumeni Syndrome 2011 - ongoing	Dana-Farber Cancer Institute (DFCI)	USA	ClinicalTrials.gov; NCT02950987	60	18 and above	• Known *TP53* mutation carrier or obligate carrier by pedigree
The LiFe-Guard study (Life-Guard) 2011 - ongoing	The Netherlands Cancer Institute	The Netherlands	-	56	18-100	• Known *TP53* mutation carrier
Toronto/Utah/CHLA LFS Study (TP-HCI)[2] 2004 - ongoing	Huntsman Cancer Institute	USA	-	54	All ages	• Known *TP53* mutation carrier
NA 2013 - ongoing	MD Anderson Cancer Center (MDACC)	USA	-	52	All ages	• Known *TP53* mutation carrier
Magnetic Resonance	Institute of	UK	ClinicalTrials.	52	18-60	• Known *TP53* mutation carrier

Imaging screening in Li Fraumeni Syndrome: An exploratory whole body MRI study (SIGNIFY)[3] 2012 - ongoing	Cancer Research		gov Identifier: NCT01737255			(known low penetrance mutations excluded) • No previous malignancy diagnosed < 5 years ago; • No current symptoms suggestive of malignancy
Toronto/Utah/CHLA LFS Study (TP-HSC&CHLA)[2] 2004 - ongoing	The Hospital for Sick Children and Children's Hospital of LA	Canada/ USA	-	36	All ages	• Known *TP53* mutation carrier
A Surveillance study in Multi-Organ Cancer prone syndromes (SMOC) (JAMA Onc in press) 2012 - ongoing	Garvan Institute of Medical Research, Peter MacCallum Cancer Centre, Monash Medical Centre	Australia	http://www.anzctr.org.au: ACTRN12613000987763	30	18-70	• Known *TP53* mutation carrier or 50% risk • No active cancer diagnosis
NA 2012 - ongoing	Texas Children's Hospital (TXCH)	USA	NA	19	0-17	• Known *TP53* mutation carrier
Cancer Genetics Registry (CGR) 2002 - ongoing	University of Michigan	USA	University of Michigan IRB Med No. HUM00043430	16	Up to 100	• Known *TP53* mutation carrier
Molecular Genetics Studies of Cancer Patients and Their Relatives (COHR) 2014 - ongoing	City of Hope Hospital	USA	www.cancergenetics.net; COH IRB #96144	11	All ages	• At risk for hereditary cancer predisposition. Known *TP53* mutation carriers under surveillance for cancer were included in the study herein.
NA 2016 - ongoing	Memorial Sloan Kettering Cancer Center (MSKCC)	USA	NA	8	18 and above	• Known *TP53* mutation carrier or obligate carrier by pedigree

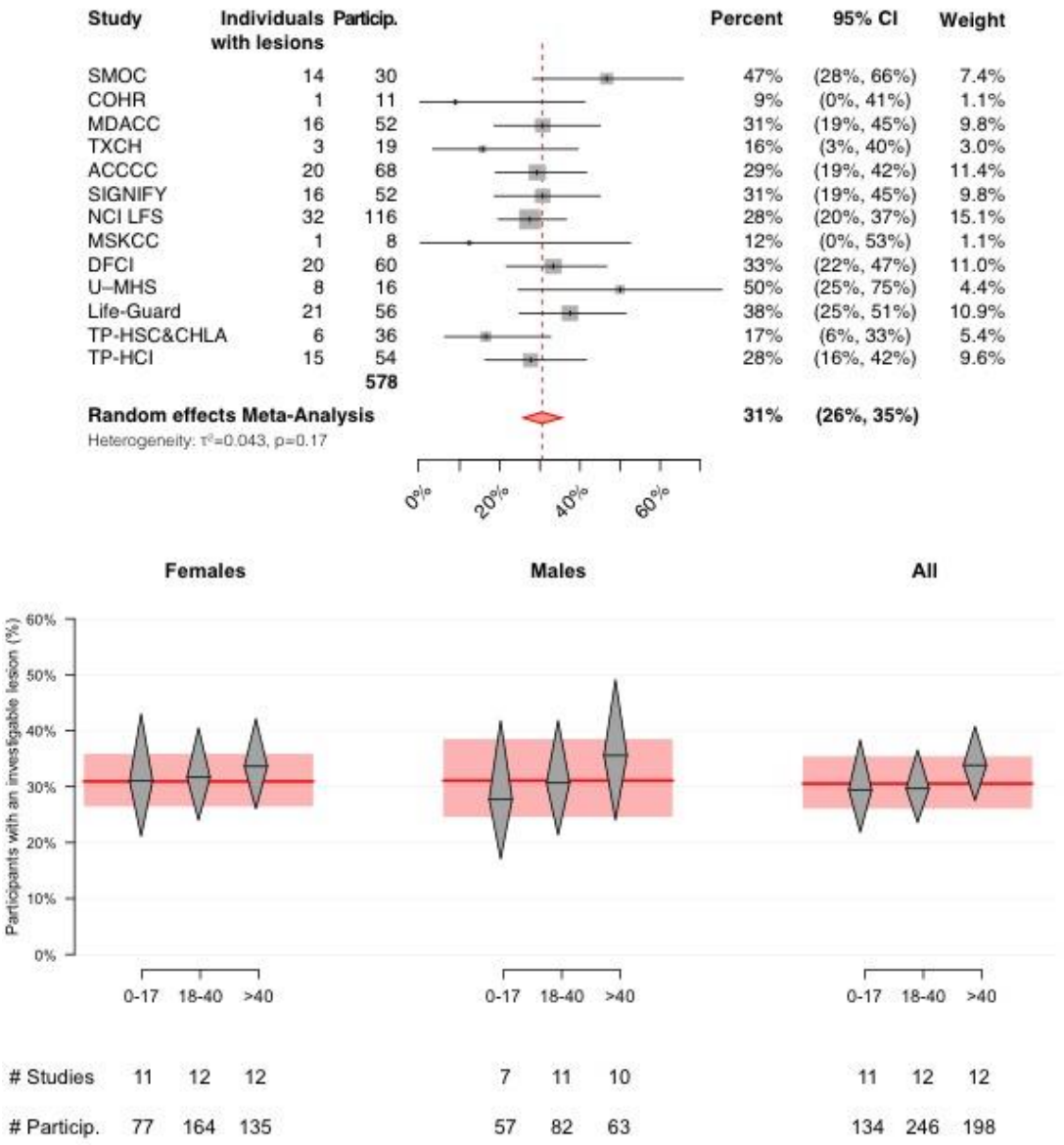

Figure 1. Meta-analysis results for the proportion of individuals found to have one or more investigable lesions. The top half of the figure presents full analysis results from all participants combined: The number of observed individuals with lesions and the total number of examined individuals from each study, study-specific proportion estimates with exact 95% confidence intervals, study weight in the meta-analysis, and a forest plot to visualize the studies in relation to one another. Immediately below are the overall proportion estimate, its approximate 95% confidence interval, and the estimated between-study heterogeneity τ^2. The lower half of the figure gives meta-analysis estimates and approximate 95% confidence intervals for each age/sex subgroup; Diamonds indicate the estimates/CIs for each subgroup by age. Bands indicate the estimates/CIs for each subgroup with age groups combined. For each age/sex subgroup, the number of studies contributing participants and the total number of participants are provided at the bottom of the figure. See Table 1 in the Supplement for cohort abbreviations.

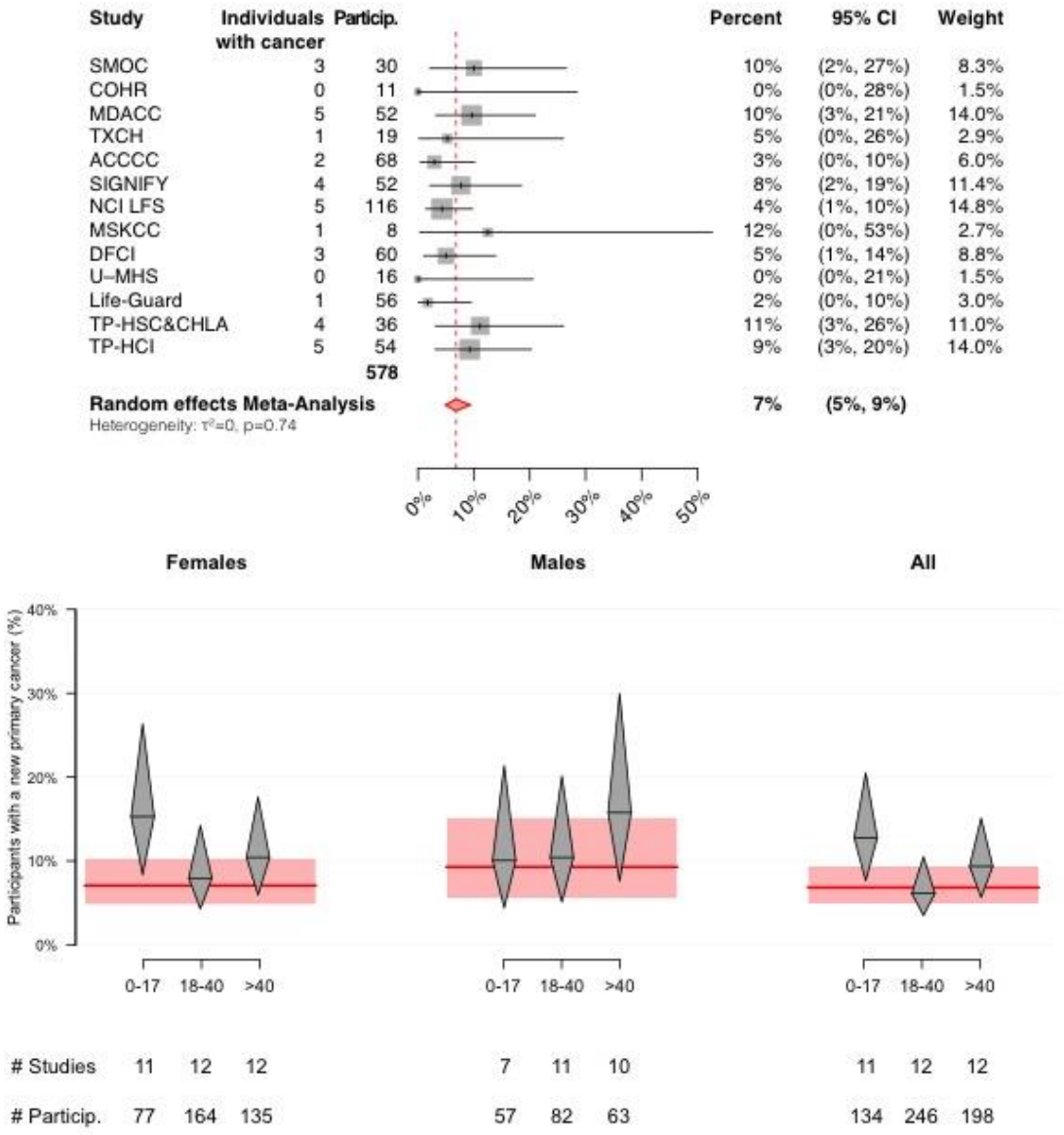

Figure 2. Meta-analysis results for the proportion of individuals found to have one or more new primary cancers. The top half of the figure presents full analysis results from all participants combined: The number of observed individuals with a new primary cancer and the total number of examined individuals from each study, study-specific proportion estimates with exact 95% confidence intervals, study weight in the meta-analysis, and a forest plot to visualize the studies in relation to one another. Immediately below are the overall proportion estimate, its approximate 95% confidence interval, and the estimated between-study heterogeneity τ^2. The lower half of the figure gives meta-analysis estimates and approximate 95% confidence intervals for each age/sex subgroup; Diamonds indicate the estimates/CIs for each subgroup by age. Bands indicate the estimates/CIs for each subgroup with age groups combined. For each age/sex subgroup, the number of studies contributing participants and the total number of participants are provided at the bottom of the figure. See Table 1 in the Supplement for cohort abbreviations.

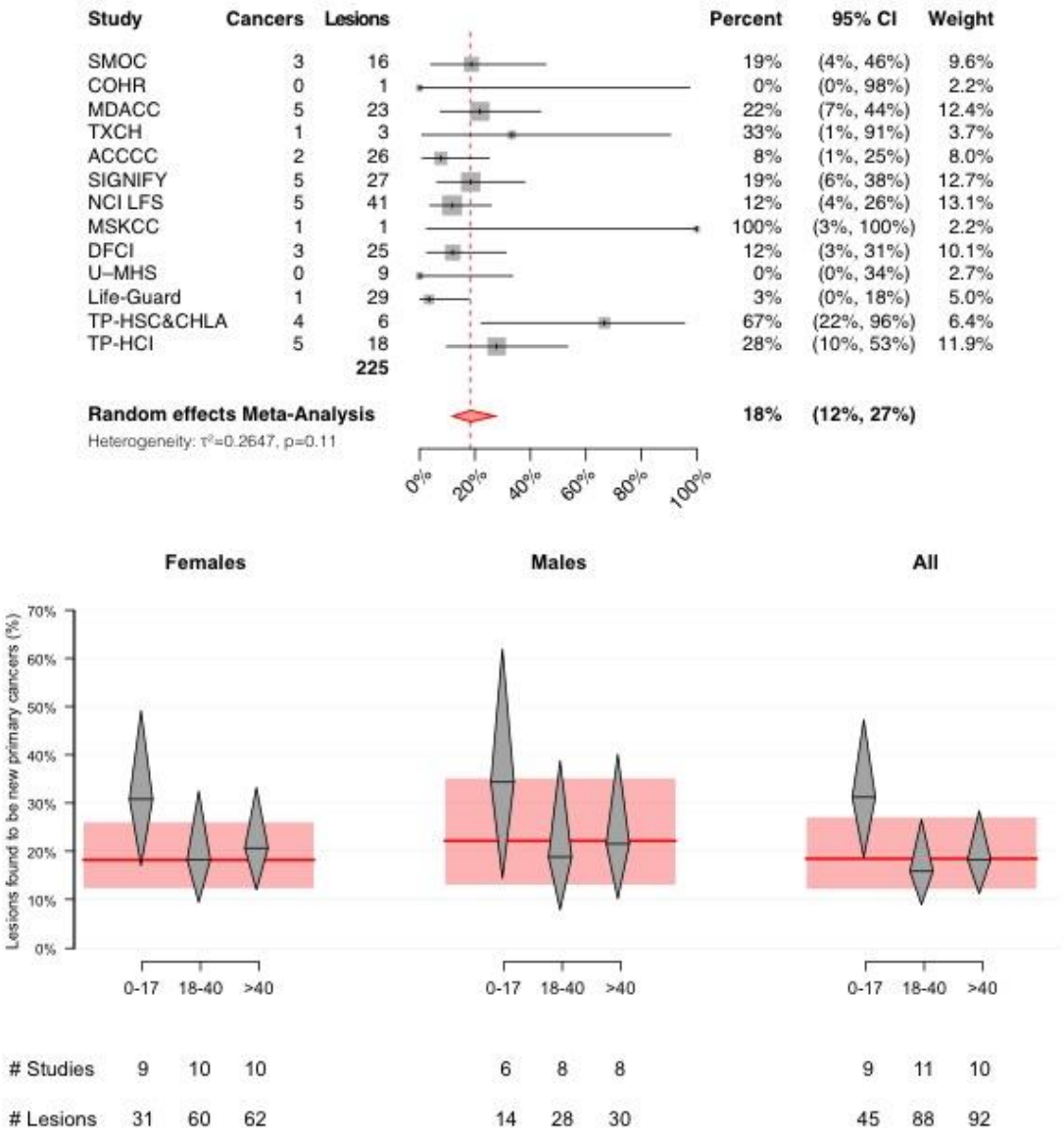

Figure 3. Meta-analysis results for the proportion of identified lesions found to be a new primary cancer. The top half of the figure presents full analysis results from all participants combined: The number of observed cancer and the total number of observed lesions from each study, study-specific proportion estimates with exact 95% confidence intervals, study weight in the meta-analysis, and a forest plot to visualize the studies in relation to one another. Immediately below are the overall proportion estimate, its approximate 95% confidence interval, and the estimated between-study heterogeneity τ^2. The lower half of the figure gives meta-analysis estimates and approximate 95% confidence intervals for each age/sex subgroup; Diamonds indicate the estimates/CIs for each subgroup by age. Bands indicate the estimates/CIs for each subgroup with age groups combined. For each age/sex subgroup, the number of studies with observed lesions and the total number of observed lesions are provided at the bottom of the figure. See Table 1 in the Supplement for cohort abbreviations.

Table 2. New primary brain tumours detected by dedicated brain MRI

Age group (yr)	Gender	Morphology, age at detection (yrs)	Treated with curative intent	Detected on WBMRI also?
0-17	Male	Low grade glioma, 11	Yes	No
		Low grade glioma, 15	Yes*	Yes
		Astrocytoma, 10	Yes	Not performed
	Female	CPC, 1	Yes	Not performed
		CPC, 4	Yes	Yes
		Low grade glioma, 4	Yes	No
		Low grade glioma, 6	Yes*	Yes
		Low grade glioma, 9	Yes	No
		Low grade glioma, 13	Yes*	Yes
		Astrocytoma, 13	Yes	Yes
		Astrocytoma, 11	Yes	Not performed
18-40	Female	Low grade glioma, 24	No	No
		Astrocytoma, 29	Yes	No

CPC, Choroid plexus carcinoma; WBMRI, whole body magnetic resonance imaging:
*Currently under surveillance with short interval MRI, with the intent to resect at a later stage

Table 3. NCI LFS Study WBMRI imaging protocol

	Coronal stir—WHOLE BODY	***Coronal T1 GRE—WHOLE BODY***	***AXIAL DIFFUSION—CHEST ABD PELVIS ONLY***	***STIR AXIAL - WHOLE BODY***	***Axial 3D Vibes—Chest Abd Pelvis:Pre/Post***
MRI instrument	Siemens Aera 1.5T	Siemens Aera 1.5T	Siemens Aera 1.5T	Siemens Aera 1.5T	Siemens Aera 1.5T
MR imaging sequence	TSE	3D T1	EPI-DWI	TSE	3d VIBE/GRE
Coverage	HEAD>TOES	HEAD>TOES	CHEST/ABD/ PEL	WHOLE BODY	C/A/P
Contrast agent	NONE	NONE	NONE	NONE	YES: SINGLE DOSE Gadavist
No of slice partitions	VARIABLE	VARIABLE	VARIABLE	VARIABLE	VARIABLE
Technique	TSE-IR	3D VIBE-GRE	DWI	TSE-STIR	VIBE/GRE
Orientation	CORONAL	CORONAL	AXIAL	AXIAL	AXIAL
Field of view	400 cm	400	36CM	36cm	36cm
Matrix size	448 X 70%	336 x 448	128 X 128	256 x 192	320 x 240
TR	~4,000mSec	6mSec	9000 mSec	5000 mSec	3.7 msec
TE	60	4.7 mSec	62 mSec	61 mSec	1.81msec
Echo-planar imaging factor		None	124		-
TSE imaging factor	11			14	
Parallel imaging factor	2	2	2	2	2
No of signals averaged	Between 1-4	1	4	VARIABLE	1
Section thickness	10	3.5	6mm	5mm	3mm
Direction of motion probing gradients	-	-	-	-	-
Receiver bandwidth	250 hz/px	700 hz/px	1500 hz/px	285 hx/px	505 hz/px
Fat suppression	IR pulse: 160	none	YES	IR pulse: 160	yes
b-values (s/mm2)	none	n/a	800	n/a	none

Table 4. City of Hope WBMRI imaging protocol

	T1 Coronal VIBE Pre-Contrast	STIR Coronal	Axial Diffusion B 50/800	T2 Axial HASTE	T1 Axial VIBE Pre and Post contrast	T1 Coronal VIBE Post contrast
Instrument	Siemens 3T	Siemens 3T	Siemens 3T	Siemens 3T	Siemens 3T	Siemens 3T
Coverage	Whole body incl brain	Whole body incl brain	Whole body incl brain	Whole body incl brain	Whole body incl brain	Whole body incl brain
Contrast	Gadolinium (MultiHance)	Gadolinium (MultiHance)	Gadolinium (MultiHance)	Gadolinium (MultiHance)	Gadolinium (MultiHance)	Gadolinium (MultiHance)
TR (ms)	3.92	3560	8500	800	4.59	3.92
TE (ms)	1.36	105	75	85	2.05	1.36
TI (ms)	-	200	200	-	-	-
FOV (mm)	440	440	440	440	360	440
Signal Averages	1	1	5	1	1	1
FA (deg)	9	125	-	150	9	9
Phase matrix	224	276	86	224	224	224
Freq matrix	320	384	120	320	320	320
Slice thickness (mm)	5	5	85	6	3	5
Slice gap (mm)	0	1	0	1	0	0
Bandwidth (Hz/Px)	390	334	2314	401	400	390
# of slices	36	36	32	26	64	36
Parallel imaging factor	2	2	2	2	2	2
Diff directions	-	-	3	-	-	-
Fat suppression	None	-	SPAIR	-	Q-Fat Sat	Q-Fat Sat
EPI factor	-	-	86	-	-	-

Table 5. The Life-Guard Study WBMRI imaging protocol

MRI Instrument	Philips Achieva dStream 3T	Philips Achieva dStream 3T	Philips Achieva dStream 3T
MR imaging sequence	T1	T2-STIR	DWIBS
Coverage	WB *	WB*	WB[$]
Contrast agent (provide details)	no	no	no
No of slice partitions / packages	3	4	2
Technique	TSE	IR-TSE	EPI-DWI
Orientation	coronal	coronal	axial (MPR-> coronal
Field of view FHxRLxAP mm	310 x 449 x 230	310 x 449 x 230	359 X 450 x 342
Matrix size	196 x 240	196 x 246	100 x 66
TR ms	561	6884	9425
TE ms	8	70	57
TSE factor	3	single shot	-
Echo-planar imaging factor	-	-	single shot
Parallel imaging factor / Sense factor	4 (LR)	4 (LR)	2.5 (AP)
No of signals averaged	1	1	3
Section thickness /slice thickness	6 mm	6 mm	6 mm
Direction of motion probing gradients	-	-	gradient overplus
Receiver bandwidth / water fatshift pixels	0.429 pixel	1.137 pixel	4.037 pixel
Fat suppression	no	STIR	STIR
b-values (s/mm2)	-	-	b = 1000

* in 7 stations: feet, lower legs, knee, upper legs, abdomen, thorax, head
[$] in 3 stations: neck-thorax, abdomen, pelvis

Table 6. Baylor College of Medicine/Texas Children's Cancer Center

	WBMRI (Abd/pel)	WBMRI (Abd/pel)	WBMRI (Abd/pel)	WBMRI (Femur)	WBMRI (Femur)	WBMRI (Lower leg)	WBMRI (Lower leg)
MRI instrument	XL Torso	XL Torso	XL Torso	Q BODY COIL	Q BODY COIL	Q BODY COIL	Q BODY COIL
MR imaging sequence	T2	T2	STIR	T1	STIR	T1	STIR
Coverage	Abdomen/ Pelvis	Abdomen/ Pelvis	Abdomen/ Pelvis	FEMUR	FEMUR	LEG	LEG
Contrast agent (provide details)	n/a	n/a	n/a	NO	NO	NO	NO
No of slice partitions	30	40	30	29	29	23	23
Technique	Single Shot	Respiratory triggered	Free Breath	TSE	TSE	TSE	TSE
Orientation	Coronal	Axial	Coronal	COR	COR	COR	COR
Field of view	460	440	460	480	480	370	370
Matrix size	276 X 283	340 X 156	228 X 187	320 X 268	340 X 200	336 X 244	252 X 158
TR	1500	1500	2500	580	4100	500	3500
TE	80	95	20	7	15	7	15
Echo-planar imaging factor	n/a	n/a	n/a	NO	NO	NO	NO
Parallel imaging factor	2	1.5	1.5	NO	NO	NO	NO
No of signals averaged	1	2	2	1	2	1	2
Section thickness	6	5	6	5	5	5	5
Direction of motion probing gradients	RL	AP	RL	RL	RL	RL	RL
Receiver bandwidth	644.1	207.1	336.1	217.8	309.6	218	293.9
Fat suppression	none	yes	yes	NO	YES/ STIR	NO	YES/ STIR
b-values (s/mm2)	n/a	n/a	n/a	NO	NO	NO	NO

Table 7. MD Anderson Cancer Centre WBMRI imaging protocol

MRI instrument	Siemens Aera 1.5T						
MR imaging sequence	Scout	DWI	T2 TIRM	T1FS Post VIBE			T1FS Post
Coverage	Vertex to toes	Vertex to toes	Vertex to toes	Head	Chest to pelvis	Thighs to toes	Total Spine
Contrast agent	None			0.1 mmol/kg of gadobutrol 7.5 mmol/7.5 mL			
No of slice partitions	7	5	6	1	3	3	2
Technique	SE, 2D	TRACE	IR, 2D	FS, 3D	FS, 3D	FS, 3D	FS, 2D
Orientation	Coronal	Axial	Coronal	Axial	Axial	Axial	Sagittal
Field of view (cm)	45 x 45	45 x 45	45 x 45	24 x 24	44 x 44	38 x 38	34 x 34
Matrix size	320x256	160x108	384x207	256x192	384x171	288x132	320x256
TR	1500	8300	5130 (H&n) 3000 (ch/ab) 5500 (pel-toes)	12	4.09 (ch) 4.38 (ab) 4.51 (pel)	4.51	<500
TE	90	66	58 (H&N) 75 (ch/ab) 54 (pel-toes)	2.38	1.72 (ch) 1.96 (ab) 1.9 (pel)	1.9	~10
Echo-planar imaging factor (EPI Factor in Siemens)	192	108	15 (H&N) 25 (ch/ab) 9 (pel-toes)	N/A	N/A	N/A	3
Parallel imaging factor	2	N/A	2	2	2	2	2
No of signals averaged	1	6	1	2	1	1	3
Section thickness	6	5	6 (chest/ab) 5 (others)	5	5	5	4
Receiver bandwidth	710	1736	233 (head and neck) 260 (chest/ab) 289 (others)	220	540	420	220
Fat suppression	No	No	Yes	Yes	Yes	Yes	Yes
b-values (s/mm2)	N/A	50, 400	N/A	N/A	N/A	N/A	N/A

Table 8. MSKCC WBMRI imaging protocol

Instrument	GE 750W	GE 750W	GE 750W	GE 750W	GE 750W	GE 750W	GE 750W
MR imaging sequence	T1FLAIR	FRFSE-XL	FSE-IR	SSFSE	DWI	LAVA-FLEX	LAVA-
Coverage	Upper & Lower	Upper & Lower	Upper/mid/ low	Chest/ abd/pel	Whole body	Whole body	Liver
Contrast agent (provide details)	NA	NA	NA	NA	NA	PRE & POST	Multiphase /Portal venous
No of slice partitions	16	16	60-70	48	36 PER SERIES	32	60
Technique	SEQ, EDR, TRF	FC,EDR, TRF	NPW/FC/ EDR/ARC/ TRF	EDR,SS, ARC	ASSET/ EDR/IR PREP	EDR/ ZIP2/ ZIP512	EDR/ZIP2/ ZIP512/ ASSET/ FLUORO
Orientation	Sagittal	Sagittal	Coronal	Axial	Axial	Axial	Axial
Field of view	32-36	32-36	40-44	40-44	48	48	36-40
Matrix size	320/224	320/224	320/192	320/192	96/128	256/160	320/192
TR	2000	2000	3000-5000	2500	4500	MIN	MIN
TE	22	22	42	100	MIN	MIN	MIN
Echo-planar imaging factor	N	N	N	N	N	N	N
Parallel imaging factor	N	N	2	2	2	N	2
No of signals averaged	1	1	1	NA	2 &10	1	N
Section thickness	4	4	4	5	5	8	5
Direction of motion probing gradients	AP	AP	RL	AP	AP	AP	AP
Receiver bandwidth	41.67	41.67	41.67	83.33	250	142.86	62.5
Fat suppression	N	Y	N	N	N	N	Y
b-values (s/mm2)	N	N	N	N	50&900	N	N

Table 9. SIGNIFY WBMRI imaging protocol

MRI instrument	1.5T	1.5T	1.5T	1.5T
MR imaging sequence	T1-weighted gradient echo	Fat suppressed T2-weighted HASTE	DWIBS Whole body diffusion weighed MR imaging with background signal suppression	T1-weighted VIBE DIXON
Coverage	vertex to feet	vertex to feet	vertex to feet	vertex to feet
Contrast agent	none	none	none	none
No of slice partitions	30	30	30 image sections per stack	52
Technique	Breath-hold	Breath-hold	Free breathing	Breath-hold
Orientation	Axial	Axial	Axial	Coronal
Field of view	38-40cm	38-40cm	38-40cm	38-40cm
Matrix size	182 x 320	208 x 256	128 x 128	192x192
TR	247	1000	8600	6.97
TE	4.36	84	72	2.39
Flip angle	70	180	NA	NA
Voxel size (mm)	1.2 x 1.2 x 8	1.5 x 1.5 x 8	1.5 x 1.5 x 8	1 x 1 x 5
Echo-planar imaging factor			150	
Parallel imaging factor	2	2	2	3
No of signals averaged	1	1	4	1
Section thickness	8	8	8	5
Direction of motion probing gradients	None	None	3 scan trace	None
Receiver bandwidth	300	501	1954	450
Fat suppression	None	SPAIR	STIR (T1=180ms)	None
b-values (s/mm2)	NA	NA	Typically 50 and 800-1000	NA

Table 10. TORONTO Protocol – HSK & CHLA WBMRI imaging protocol

SCANNER	**PHILIPS ACHIEVA**	
FIELD STRENGTH	**1.5T**	
MR imaging sequence	SCOUT- T1 FFE (GRADIENT)	STIR
Coverage	Head to foot/vertex to heel	Head to foot/vertex to heel
Contrast agent	NO	NO
***No of slice partitions**	6	6
Technique	2D	2D
Orientation	3 PLANE	COR
***Field of view**	53 CM	53 CM
***Matrix size**	512 x 410	380 x 297
***TR**	13.9348	2769.9
***TE**	3.457	60
Echo-planar imaging factor	N/A	N/A
Parallel imaging factor	1	1
No of signals averaged	1.5T	8
***Section thickness**	265	5
***Slice gap**	0	1
Direction of motion probing gradients	3 PLANES	H-F
Receiver bandwidth	198	446
Fat suppression	NO	YES - STIR
b-values (s/mm2)	N/A	N/A
Coil	Body Quadrature	Body Quadrature

*Patient specific; STIR, short tau inversion recovery; N/A, not applicable

Table 11. AC Camargo Cancer Centre WBMRI imaging protocol

MRI instrument	1.5T instrument (Signa Excite HD; GE Healthcare, Milwaukee, USA)
MR imaging sequence	T1; stir; DWI
Coverage	Tip to toe
Contrast agent (provide details)	NONE
Technique	rapid whole body MRI
Orientation	coronal and axial
Field of view*	approximately 30 cm
Matrix size*	approx. 312
TR*	different for T1; stir; DWI
TE*	different for T1; stir; DWI
Parallel imaging factor	0
Section thickness	5mm
Direction of motion probing gradients	3 Dimensional valid for DWI
Fat suppression	yes in DWI and STIR(saturated imaging recovery)
b-values (s/mm2)	800mm2/s

Table 12. SMOC WBMRI imaging protocol

	T1-weighted gradient echo	**Fat-suppressed T2-weighted HASTE**	**DWIBS Whole body diffusion weighted MR imaging with background signal suppression**	**T1-weighted VIBE DIXON**
Instrument	Siemens MAGNETOM Trio 3T or Siemens 1.5 T Avanto	Siemens MAGNETOM Trio 3T or Siemens 1.5 T Avanto	Siemens MAGNETOM Trio 3T or Siemens 1.5 T Avanto	Siemens MAGNETOM Trio 3T or Siemens 1.5 T Avanto
Contrast	None	None	None	None
Coverage	Vertex to feet	Vertex to feet	Vertex to feet	Vertex to feet
No of slice partitions	30	30	30 images per stack	52
Technique	Breath-hold	Breath-hold	Free-breathing	Breath-hold
Orientation	Axial	Axial	Axial	Coronal
Field of view (cm)	38-40	38-40	38-40	38-40
Matrix size	150 x 256	150 x 256	150 x 256	192 x 192
TR	386	1400	14000	7
TE	4.8	93	72	2.38 & 4.76
Echo-planar imaging factor			150	
Parallel imaging factor	2	2	2	3
No of signals averaged	1	1	4	1
Section thickness (mm)	8	8	8	5
Direction of motion probing gradients	None	None	3 scan trace	None
Receiver bandwidth	330	475	1800	490
Fat suppression**	None	SPAIR	STIR (T1=180ms)	None
b-values (s/mm^2)	NA	NA	Typically 50 and 800-1000	NA

HASTE, half-fourier acquisition single-shot turbo spin-echo; DWIBS, diffusion weighted imaging background signal; TR, repetition time; TE, echo time ; SPAIR, spectral attenuated inversion recovery; STIR, short tau inversion recovery

The listed protocols represent the default minimum image quality required.

Table 13. Cancer Genetics Registry WBMRI imaging protocol

	COR T2W_TSE	DWIBS_ Tra_TB	e-THRIVE_ BH	SAG 3D FLAIR	STIR_Co r_TB	T1_Cor_ TB
Patient weight [kg] =	68;	68;	68;	113	113	68
SmartSelect =	yes	yes	yes;	yes;	yes;	yes;
Coil 1 (exclude) =	none	none	none	none	none	none
Uniformity =	clear	clear	synergy	clear	clear	clear
FOV						
FH (mm) =	300;	279;	300;	250;	250;	300;
RL (mm) =	441.176483;	450;	442.857147;	194.880005;	194.880005;	439.655182;
AP (mm) =	323;	365.625;	324;	250;	250;	323;
Voxel size FH (mm) =	1.10000002;		1.79999995;	1.04999995;	1.04999995;	1.29999995;
RL (mm) =	1.37136829;	3.5;	2.02794051;	0.560000002;	0.560000002;	1.455426 22;
AP (mm) =	NA	3.5;	3;	1.03734398;	1.03734398;	
Slice thickness (mm) =	8;	6;				8;
Recon voxel size (mm) =	0.656512618;	1.757812 5;	1.0251323;	0.9765625;	0.9765625;	0.858701 527;
Image shutter =		yes				
Fold-over suppression =	oversampling;	no;	oversampling;	no;	no;	oversampling;
L (mm) =	75;		75	user defined;		100
R (mm) =	75;		75	1;		100
Slice oversampling =			default		user defined;	
oversample factor =					1	
Reconstruction matrix =	672	256;	432	256;	256;	512;
SENSE =	yes	yes	yes	yes		yes
P reduction (RL) =	2	3;	2	3;	yes	2;
S reduction (AP) =			1	2;	2;	
k-t BLAST =	no	no;	no	no	no	no
Overcontiguous slices =			yes	yes;	yes;	
Stacks =	1	1;	1	1	1	1;
type =	parallel;	parallel;				parallel;
slices =	36;	40;	108	348	348	36;
slice gap =	user defined;	user defined;				user defined;
gap (mm) =	1	1;				1;
slice orientation =	coronal	transverse;	coronal	sagittal;	sagittal;	coronal;
fold-over direction =	RL;	AP;	RL;	AP;	AP;	RL;
fat shift direction =	F	P	F	F	F	F
Stack Offc. AP (P=+mm) =	40.4508896;	12.6855469;	40.4508896;	-25.4540024;	-25.4540024;	40.4508896;
RL (L=+mm) =	-4.24496841;	7.90579033;	-4.244968	4.73662567;	4.73662567;	-4.244968

			41;			41;
FH (H=+mm) =	-745.106079;	-43.0647545;	-745.106079;	3.2995317;	3.2995317;	-745.106079;
Ang. AP (deg) =	0.454734415;	0;	0.454734415;	1.62731862;	1.62731862;	0.454734415;
RL (deg) =	1.53861737;	-0;	1.53861737;	-1.34632874;	-1.34632874;	1.53861737;
FH (deg) =	-0.0246139914;	-0;	-0.0246139914;	7.00043583;	7.00043583;	0.0246139914
Free rotatable =	no;	no;	no;	no;	no;	no;
Minimum number of packages =	1;	1;				3
Multi-chunk =			no	no	no	
Slice scan order =	default	default;				interleaved;
Large table movement =	yes	yes;	yes	no;	no;	yes;
PlanAlign =	no	no	no	no	no	no
REST slabs =	0	0	0	0	0	0
Interactive positioning =	no;	no;	no;	no	no	no
Patient position =	head first;	head first;	head first;	feet first;	feet first;	head first;
orientation =	supine;	supine;	supine;	prone;	prone;	supine;
Scan type =	Imaging;	Imaging;	Imaging;	Imaging;	Imaging;	Imaging;
Scan mode =	MS;	MS;	3D;	3D;	3D;	MS;
technique =	SE;	IR;	FFE;	IR;	IR;	SE;
Modified SE =	no;					no;
Contrast enhancement =	T1;		T1;			
Acquisition mode =	cartesian;	cartesian;	cartesian;	cartesian;	cartesian;	cartesian;
Fast Imaging mode =	TSE;	EPI;	TFE;	TSE;	TSE;	TSE;
3D VIEW =				Brain FLAIR;	Brain FLAIR;	
shot mode =	multishot;	single-shot;	single-shot;	multishot;	multishot;	multishot;
TFE startup echoes =			user defined;			
(number) =			0;			
shot interval =			shortest;			
profile order =			linear;			
turbo direction =			Z;			
TSE factor =	24			182	182	5
TE spacing =	shortest			6;	6;	0;
startup echoes =	0			linear;	linear;	low_high;
profile order =	asymmetric			Y;	Y;	no
DRIVE =	no			no	no	no;
ultrashort =	no			default;	default;	default;
fid reduction =	default					
Echoes =	1	1	1	1	1	1

partial echo =	no	no;	no	no;	no;	no;
shifted echo =			no			
TE =	user defined;	shortest	shortest	shortest	shortest	user defined
(ms) =	90					8
Flip angle (deg) =	90;		7			90;
Refocusing control =	yes			yes	yes	yes
angle (deg) =	110			40	40	130
TR =	range	shortest	shortest	user defined	user defined	shortest
minimum (ms) =	2500			4800	4800	
maximum (ms) =	4000					
Halfscan =	no	no	yes	no	no	yes
factor =						0.699999988
factor Y =			1			
factor Z =			0.850000024			
Water-fat shift =	user defined	minimum	user defined	maximum	maximum	minimum
(pixels) =	1.5		0.600000024;			
IR delay (ms) =		220		1650	1650	
acquire during delay =		yes				
dual =		no		no	no	
power =		1		1	1	
RF Shims =	fixed	fixed	fixed	fixed	fixed	fixed
Shim =	default	auto	auto	default	default	auto
mDIXON =	no	no	no	no	no	no
Fat suppression =	no	no	SPAIR	SPIR	SPIR	no;
Grad Rev Fat suppression =		no;	1			
power =						
strength =				strong	strong	
inversion delay =			shortest;			
frequency offset =			user defined;	default;	default;	
offset (Hz) =			220;			
Water suppression =	no	no	no;	no;	no;	no;
BB pulse =	no					no
TFE prepulse =			no			
MTC =	no	no	no	no	no	no
Zoom imaging =	no					no
T2prep =			no	yes	yes	
echo time (ms) =				125;	125;	
refocusing pulses =				4;	4;	
Zoom imaging =				no	no	
Diffusion mode =	no	DWI;	no	no;	no;	no;
gradient overplus =		yes;				

nr of b-factors =		1;				
max b-factor =		800;				
average high b =		yes;				
SAR mode =	high;	high;	high;	high;	high;	high;
B1 mode =	default;	default;	default;	default;	default;	default;
PNS mode =	low;	high;	high;	high;	high;	moderate;
Gradient mode =	maximum;	maximum;	maximum;	maximum;	maximum;	default;
SofTone mode =	no;	no;	no;	no;	no;	no;
Cardiac synchronization =	no;	no;	no;	no;	no	no;
Respiratory compensation =	no;	no;	no;	no;	no	no;
Navigator respiratory comp =	no;	no;	no;	no;	no	no;
Flow compensation =	yes	no	no	no;	no;	no;
direction =	in-plane					
fMRI echo stabilisation =			no;			
Temporal slice spacing =	default;					default
Motion smoothing =	yes			no;	no;	no;
NSA =	1	3	1	2	2	1
partial NSA =				no;	no;	
SMART =		no		no	no	
Angio / Contrast enh. =			contrast enh.;			
Quantitative flow =			no;			
CE profile order =			linear;			
Manual start =	no	no	no	no	no	no
Dynamic study =	no	no	no	no	no	no
Arterial Spin labeling =	no;	no;	no;	no	no	no
Preparation phases =	auto	auto	auto	auto;	auto;	auto;
Interactive F0 =	no	no	no	no;	no;	no;
B0 field map =	no	no	no;	no	no	no
MIP/MPR =	no	no	no;	no	no	no
SWIp =			no			
Images =	M, (3) "no";	M, (3) "no";	M, (3) "no";	M, (3) "no";	M, (3) "no";	M, (3) "no";
Autoview image =	M;	M;	M;	M;	M;	M;
Calculated images =	(4) "no";		(4) "no";			(4) "no";
Reference tissue =	Skeletal muscle;	Spleen;	Lung;	Grey matter;	Grey matter;	Bone marrow;
Recon compression =	No;	No;	No;	No;	No;	No;
Preset window contrast =	soft;	intermediate;	soft;	soft	soft	soft
Reconstruction mode =	real time	immediate	real time;	real time;	real time;	real time;
Save raw data =	no	no	no			no
Hardcopy protocol =	no	no	no	no;	no;	no;
Image filter =	system default	system default	system default	system default;	system default	system default;

Geometry correction =	default	default	default	default;	default;	default;
Elliptical k-space shutter =			default;	default	default	
IF_info_seperator =	1634755923;	1634755923;	1634755923;	1634755923;	1634755923;	1634755923;
Total scan duration =	01:14.2;	02:16.9;	00:29.7;	04:43.2;	04:43.2;	01:31.1;
Rel. SNR =	1;	1	1	1	1	1;
Act. TR (ms) =	2749;					920;
Act. TR/TI (ms) =		7204 / 220;		4800 / 1650;	4800 / 1650;	
Act. TR/TE (ms) =			2.9 / 1.37;			
Time to k0 =			00:15.5;			
Act. TE (ms) =	90	66		329	329	8
ACQ matrix M x P =	272 x 285;	128 x 104;	168 x 218;	240 x 240;	240 x 240;	232 x 301;
ACQ voxel MPS (mm) =	1.10 / 1.54 / 8.00;	3.52 / 3.52 / 6.00;	1.79 / 2.03 / 6.00;	1.04 / 1.04 / 1.12;	1.04 / 1.04 / 1.12;	1.29 / 1.46 / 8.00;
REC voxel MPS (mm) =	0.66 / 0.66 / 8.00;	1.76 / 1.76 / 6.00;	1.03 / 1.03 / 3.00;	0.98 / 0.98 / 0.56;	0.98 / 0.98 / 0.56;	0.86 / 0.86 / 8.00;
Scan percentage (%) =	71.3754654;	100;	88.0239487;	100;	100;	88.7550201;
Packages =	3	1				3
TFE factor =			59			
Min. slice gap (mm) =	8;	0				8;
Optimal slices =	24;					
EPI factor =		35				
WFS (pix) / BW (Hz) =	0.681 / 638.2;	6.501 / 66.8;		0.442 / 982.7;	0.442 / 982.7;	0.508 / 855.2;
Full flow comp. =	yes;					
TFE dur. shot / acq (ms) =			191.9 / 171.4;			
TSE es / shot (ms) =	5.5 / 131;			3.3 / 627;	3.3 / 627;	8.0 / 40;
Act. WFS (pix) / BW (Hz) =			0.601 / 722.3;			
TEeff / TEequiv (ms) =				329 / 138;	329 / 138;	
Min. WFS (pix) / Max. BW (Hz) =			0.254 / 1710.3;			
Min. TR/TI (ms) =				2427 / 50;	2427 / 50;	
Min. TR (ms) =	2749					
BW in EPI freq. dir. (Hz) =		3360.2;				
SPAIR TR (ms) =			191.894608;			
SPAIR inv. delay act./auto (ms) =			80.90 [72.07];			
SPAIR offset act./default (Hz) =			220 [220];			
SAR / local torso =	< 100 %;	< 83 %;	< 40 %;	< 18 %;	< 18 %;	< 100 %;
Whole body / level =	< 3.2 W/kg / 1st level;	< 2.7 W/kg / 1st level;	< 1.3 W/kg / normal;	< 0.5 W/kg / normal;	< 0.5 W/kg / normal;	< 3.2 W/kg / 1st level;
SED =	< 0.2 kJ/kg;	< 0.4 kJ/kg;	0.0 kJ/kg;	< 0.2 kJ/kg;	< 0.2 kJ/kg;	< 0.3 kJ/kg;

B1+rms / Coil Power =	2.29 uT / 96 %;	2.08 uT / 79 %;	1.44 uT / 38 %;	0.91 uT / 15 %;	0.91 uT / 15 %;	2.29 uT / 96 %;
Max B1+rms =	2.29 uT;	2.08 uT;	1.44 uT;	0.99 uT;	0.99 uT;	2.29 uT;
PNS / level =	59 % / normal;	96 % / 1st level;	58 % / normal;	74 % / normal;	74 % / normal;	43 % / normal;
dB/dt =	46.8 T/s;	80.2 T/s;	103.7 T/s;	105.2 T/s;	105.2 T/s;	42.0 T/s;
Sound Pressure Level (dB) =	16.2031574;	21.19575 12;	29.40430 07;	24.23621 56;	24.23621 56;	20.58822 25;

Table 14. Toronto Protocol – HCI WBMRI imaging protocol

MRI Instrument	Siemens Aera 1.5T	Siemens Aera 1.5T
MR Imaging Sequence	Axial DWI	Axial VIBE
Coverage	Corpus callosum to pubic symphysis	Liver
Contrast agent	None	None
Number of slice partitions	4 sets of 50 slices	80 slices per slab (1 slab)
Technique	DWI	VIBE
Orientation	Axial	Axial
Field of view	288 x 100	400 x 84
Matrix size	128 x 128	203 x 320
TR	7000	4.36
TE	70	1.98
Echo-planar imaging factor	128	
Parallel imaging factor	Grappa 2	Grappa 2
No of signals averaged		1
Section thickness	5mm	3mm
Direction of motion probing gradients	A to P	A to P
Receiver bandwidth	1776	400
Fat suppression	No	Q-fat sat
b-values (s/mm2)	50	400,800

Table 15. Dana Farber Cancer Institute WBMRI imaging protocol

Sequence	Parameters	Comments
LOCALIZERS		LANDMARK AT CHIN. SELECT PROTOCOL ON SCANNER MATCHED TO PATIENT'S AGE AND RUN AS IS.
COR TIRM (RESP TRIGGERED IN CHEST AND ABD AREAS)	7 AND UNDER 4/0 8 AND UP 5/0 PHASE SET H-F WITH 100% OVERSAMPLING TO PREVENT WRAP. DO NOT CHANGE. THIS PREVENTS FLOW ARTIFACTS THAT WOULD OCCUR WITH PHASE IN L-R DIRECTION	BREAK COR SEGMENTS INTO 4 SEGMENTS TYPICALLY (SEE GRAPHIC PAGE 32) BUT IF CHILD IS SMALL IT IS OK TO SCAN CHEST AND ABDOMEN TOGETHER IN ONE UNIT. 4^{TH} SEGMENT WOULD ALLOW FOR MORE LOWER LEG COVERAGE. SCAN AS MUCH AS POSSIBLE. INCLUDE ARMS.
COR T1	7 AND UNDER 4/0 8 AND UP 5/0	SAME AS COR TIRM EXCEPT PHASE IS L-R
AX TIRM (RESP TRIGGERED IN CHEST AND ABD AREAS)	7 AND UNDER 4/0 8 AND UP 5/0	HEAD/NECK, CHEST, ABDOMEN AND PELVIS ONLY UNLESS OTHERWISE INDICATED BY DIAGNOSIS. INCLUDE ARMS LATERALLY.
AX T2 HASTE	7 AND UNDER 4/0 8 AND UP 5/0	CHEST ONLY. CAN BE DONE BREATH HELD IF PATIENT IS COOPERATIVE BUT NOT NECESSARY. INCLUDE ARMS LATERALLY.
SAG MPRAGE		BRAIN. NOT MOCO SEQUENCE/ SHORTER TIME MPRAGE.
AX FLAIR		BRAIN
SAG TIRM WHOLE SPINE	3/0 ALL AGE GROUPS	ENTIRE SPINE IN TWO LARGE FOV SEGMENTS
AX DWI	5/0 ALL AGES	CHEST ABDOMEN AND PELVIS ONLY

References

1. Mai PL, Best AF, Peters JA, et al: Risks of first and subsequent cancers among TP53 mutation carriers in the National Cancer Institute Li-Fraumeni syndrome cohort. Cancer 122:3673-3681, 2016

2. Villani A, Shore A, Wasserman JD, et al: Biochemical and imaging surveillance in germline TP53 mutation carriers with Li-Fraumeni syndrome: 11 year follow-up of a prospective observational study. Lancet Oncol 17:1295-305, 2016

3. Saya S, Killick E, Thomas S, et al: Baseline results from the UK SIGNIFY study: a whole-body MRI screening study in TP53 mutation carriers and matched controls. Fam Cancer, 2017