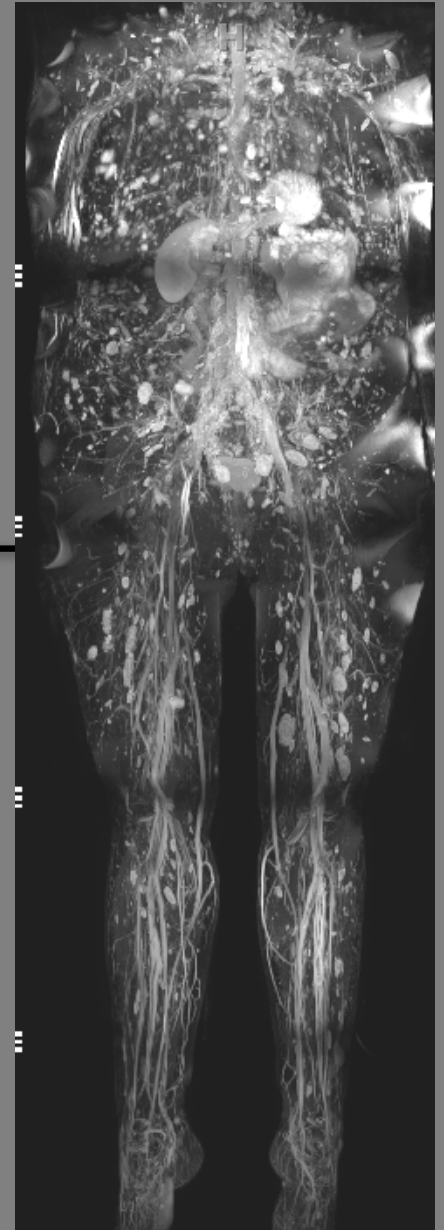


Whole Body MRI Working Group

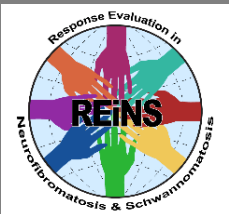
Shivani Ahlawat, MD



Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

Whole Body MRI Working Group

- Main Goal: Development of standardized methods of WB-MR image acquisition and analysis to enable its use as an endpoint in NF clinical trials.



Reilly KM, Kim A, Blakely J, Ferner RE, Gutmann DH, Legius E, Miettinen MM, Randall RL, Ratner N, Jumbé NL, Bakker A, Viskochil D, Widemann BC, Stewart DR. Neurofibromatosis Type 1-Associated MPNST State of the Science: Outlining a Research Agenda for the Future. *J Natl Cancer Inst.* 2017 Aug 1;109(8). 2

Objectives

- Review priority items of investigation for the WB-MRI working group
- Discuss the interval advances in WB-MR image acquisition
- Discuss the recent advances in WB-MR image analysis
- Discuss current WB-MRI utilization and its challenges



Table 3

Future directions for whole-body MRI (WB-MRI) investigations in patients with neurofibromatosis (NF)

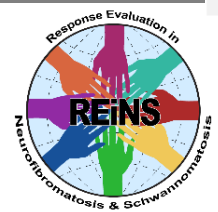
Table 3 Future directions for whole-body MRI (WB-MRI) investigations in patients with neurofibromatosis (NF)

Sensitivity, specificity, and reproducibility of WB-MRI in NF

1. Comparative study of 3.0T vs 1.5T for tumor detection
2. Comparative study for 2D vs 3D acquisition for tumor detection
3. Comparative study of axial vs coronal imaging acquisition for tumor detection
4. Comparative study of regional vs WB-MRI for tumor detection
5. Test retest variability and interobserver performance of WB-MRI in NF
6. Determination of the minimally meaningful clinical change of tumor size with WB-MRI

Biologic characterization of tumor

1. Investigate functional MRI (diffusion-weighted imaging/apparent diffusion coefficient mapping) vs other imaging modalities such as fluorodeoxyglucose PET for tumor characterization and assessment of treatment response
2. Investigate the added value of contrast-enhanced imaging to WB-MRI protocol for characterization and assessment of treatment response



Whole Body MR Image Acquisition



WB-MRI acquisition

Table 1 Imaging parameters for WB-MRI from NF-related investigations focused on detection or characterization of PNST

Publication (see references)	Technical considerations: magnet strength (1.5T vs 3T); sequences (2D vs 3D); plane of acquisition (axial, coronal, sagittal)	Specific sequences	Contrast material (+/-)	Functional DWI and ADC mapping (+/-)
10	1.5T; 2D; coronal	STIR	-	-
11	1.5T; 2D ^a	STIR: slice thickness 5-10 mm; matrix 256-512 × 256; T1; slice thickness 5-10 mm; matrix 256-512 × 256	+; Gadolinium-DTPA (Magnevist, Bayer Schering Pharma AG, Germany)	-
12	1.5T; 2D; coronal	STIR: TR/TE/IR 4,190/111/150; echo train length 25; FOV 50 cm; matrix 320 × 240; slice thickness 10 mm; no interslice gap	-	-
13	3.0T; 3D; coronal	Pre and post contrast VIBE: TR/TE 0.88/2/43 ms; FOV 50 cm ² ; matrix 256 × 256; slice thickness 2 mm; STIR: TR/TE 6,640/84 ms; FOV 50 cm ² ; matrix 256 × 256; slice thickness 2 mm with interpolation	+; 0.1 mmol/kg gadodiamide contrast agent (Magnevist, Bayer Schering Pharma AG, Germany)	+; TR/TE 4,100/70 ms; b values 50, 400, 800 s/mm ² ; FOV 50 cm ² ; slice thickness 5 mm
14	1.5T; 2D; coronal and axial	STIR: axial; TR/TE 3,690 ms/106 ms; FOV 25.7 × 50.0 cm; coronal; TR/TE 3,110 ms/101 ms; FOV 48 cm ² ; T1W FS pre and post contrast: axial; TR/TE 91 ms/4.76 ms; FOV 47.9 cm ²	0.1 mmol/kg or 0.2 mmol/kg bodyweight gadolinium-DTPA	-
15	1.5T; 2D ^a	STIR: slice thickness 10 mm; no interslice gap	-	-
16	1.5T; 2D; coronal	STIR: TR/TE/IR 4,190/111/150; slice thickness 10 mm; no interslice gap; FOV 50 cm ² ; echo train length 25; matrix 320 × 240	-	-
17	1.5T; 2D; axial	STIR: slice thickness 10 mm	-	-
18	1.5T; 2D; axial	STIR: slice thickness 10 mm	-	-
19	1.5T; 2D; coronal	STIR: TR/TE/IR 4,190/111/150; slice thickness 10 mm; no interslice gap; FOV 50 cm ² ; echo train length 25; matrix 320 × 240	-	-
20	1.5T; 2D; coronal and axial	Axial: T1 (slice thickness 6-12 mm); T2 FS (slice thickness 6-12 mm); coronal: T1 (slice thickness 5-10 mm); T2 FS (slice thickness 5-10 mm)	-	-
21	1.5T; 2D; coronal and axial	T1SE: slice thickness 5-10 mm; no interslice gap; STIR: slice	-	-



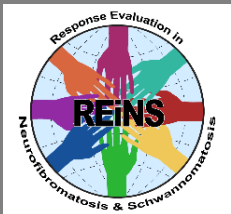
WB-MRI acquisition

Center	Technical considerations	Specific Sequence	Contrast	DWI/ADC mapping
MGH	3D	Volumetric fluid sensitive & T1-pre In-phase and opposed-phase	-	DWI/ADC
NCI	2D	Axial and coronal STIR	-	+/- DWI/ADC – special cases – localized MRI
Manchester	2D	Fluid sensitive	-	
Hamburg	2D	Axial and coronal STIR	-	+/- DWI/ADC – special cases
Hopkins	3D	STIR & Volumetric fluid sensitive & T1-pre	+	DWI/ADC



Challenge

- Development of standardized WB-MR techniques is challenging due to advances in technology and the dynamic nature of imaging protocols

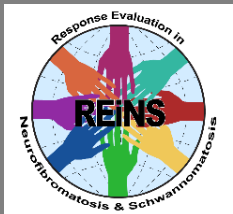


WB-MRI acquisition

Test-retest WB-MRI variability and inter-observer performance –
planned



Whole Body MR Image Analysis



WB-MRI analysis

Volumetric MRI Analysis of Plexiform Neurofibromas in Neurofibromatosis Type 1: Comparison of Two Methods

Wenli Cai, PhD, Seth M. Steinberg, PhD, Miriam A. Bredella, MD, Gina Basinsky, MD, Bhanusupriya Somarouthu, MD, Scott R. Plotkin, MD, PhD, Jeffrey Solomon, PhD, Brigitte C. Widemann, MD, Gordon J. Harris, PhD, Eva Dombi, MD

Objectives: Plexiform neurofibromas (PNs) are complex, histologically benign peripheral nerve sheath tumors that are challenging to measure by simple line measurements. Computer-aided volumetric segmentation of PN has become the recommended method to assess response in clinical trials directed at PN. Different methods for volumetric analysis of PN have been developed. The goal of this study is to test the level of agreement in volume measurements and in interval changes using two separate methods of volumetric magnetic resonance imaging analysis.

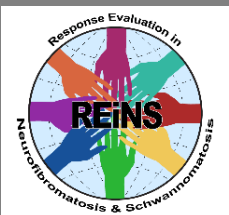
Methods: Three independent volume measurements were performed on 15 PN imaged at three time-points using 3DQI software at Massachusetts General Hospital (MGH) and National Cancer Institute (NCI) and MEDx software at NCI.

Results: Median volume differences at each time-point comparing MGH-3DQI and NCI-3DQI were -0.5 , -4.2 , and -19.9 mL; comparing NCI-3DQI and NCI-MEDx were -21.0 , -47.0 , and -21.0 mL; comparing MGH-3DQI and NCI-MEDx were -10.0 , -70.3 , and -29.9 mL. Median differences in percentage change over time comparing MGH-3DQI and NCI-3DQI were -1.7 , 1.1 , and -1.0% ; comparing NCI-3DQI and NCI-MEDx were -2.3 , 3.3 , and -1.1% ; comparing MGH-3DQI and NCI-MEDx were -0.4 , 2.0 , and -1.5% . Volume differences were $<20\%$ of the mean of the two measurements in 117 of 135 comparisons (86.7%). Difference in interval change was $<20\%$ of the 135 comparisons (88.9%), while disease status classification was concordant in 115 of 135 comparisons (85.2%).

Conclusions: The volumes, interval changes, and progression status classifications were in good agreement. The comparison of two volumetric analysis methods suggests no systematic differences in tumor assessment. A prospective comparison of the two methods is planned.

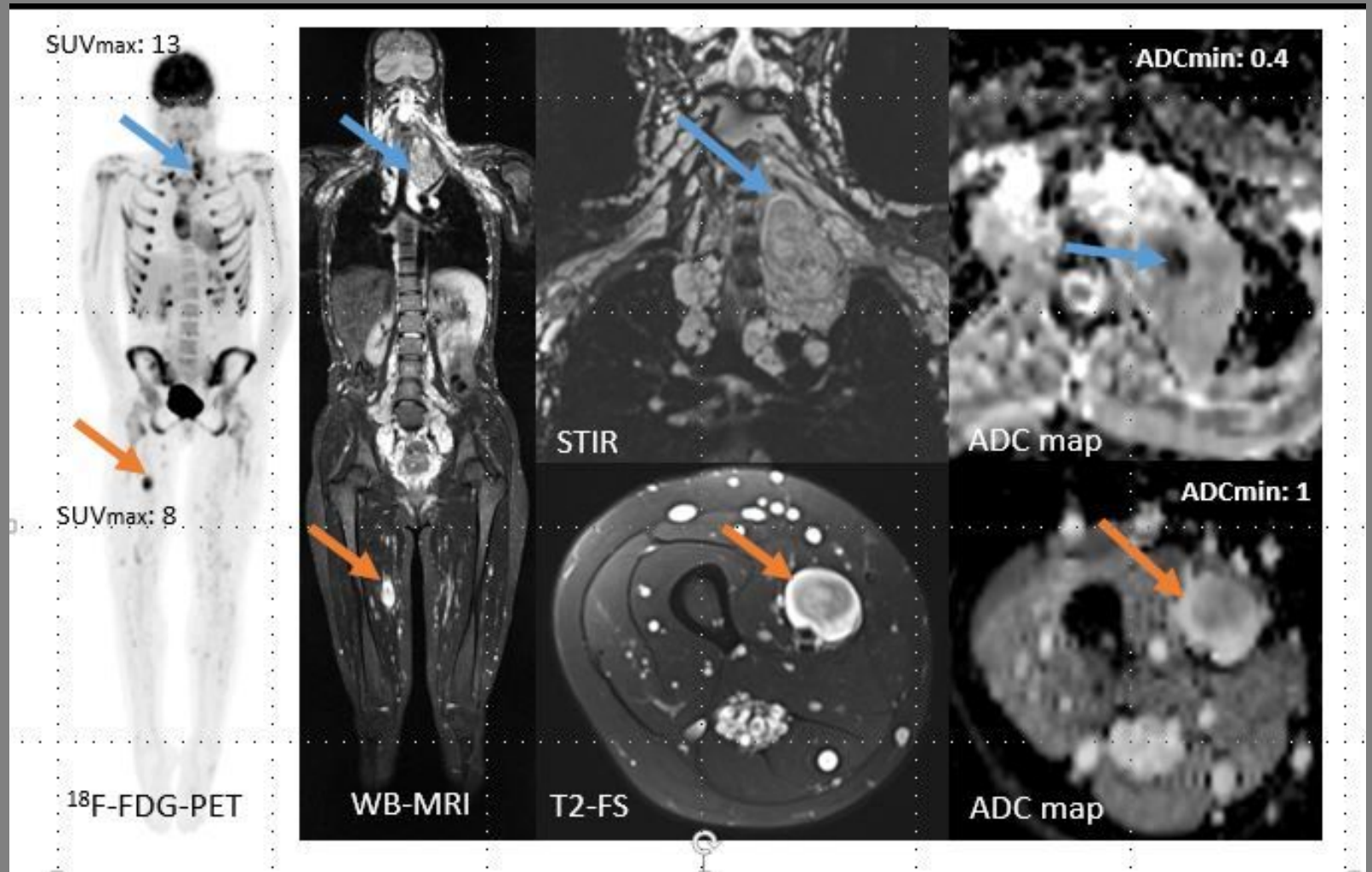
Key Words: Neurofibromatosis type 1; plexiform neurofibroma; tumor response evaluation; volumetric MRI.

Published by Elsevier Inc. on behalf of The Association of University Radiologists.



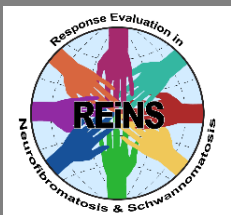
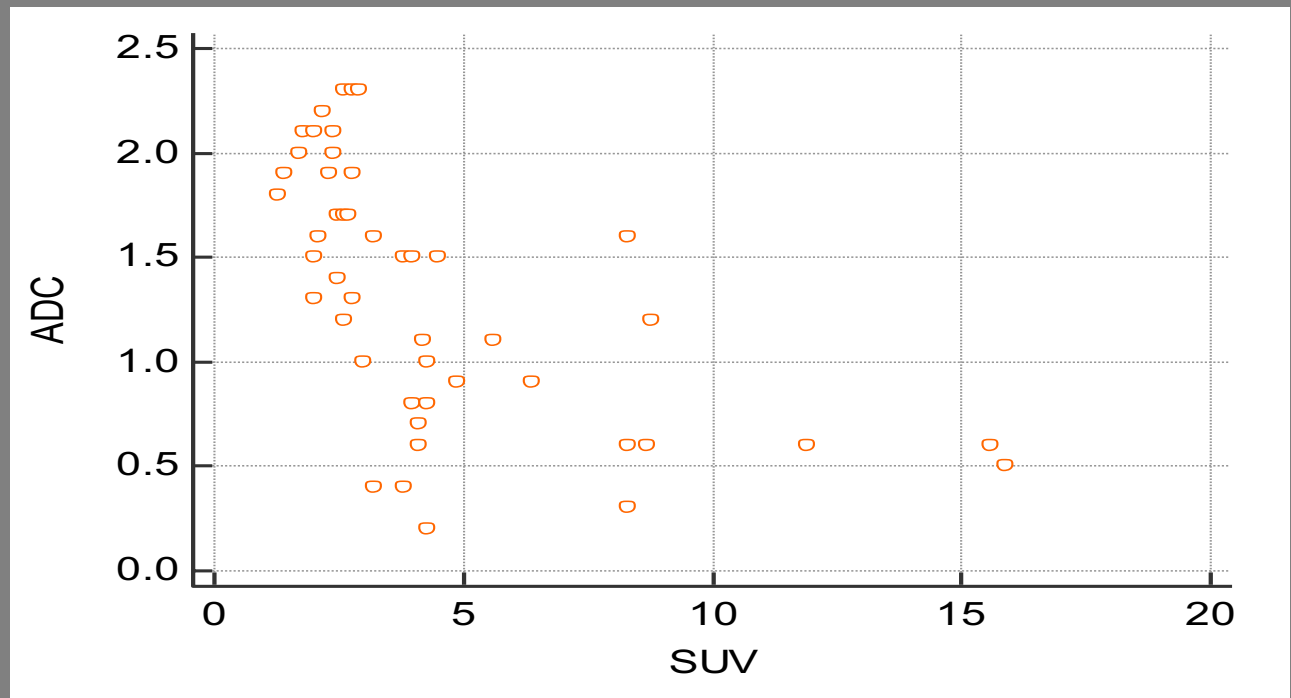
WB-MRI analysis

Whole Body metabolic v functional imaging strategies



WB-MRI analysis

Variable Y	ADC
Variable X	SUV
Sample size	47
Correlation coefficient r	-0.5827
Significance level	P<0.0001
95% Confidence interval for r	-0.7452 to -0.3549



Whole Body MR Image Utilization



WB-MRI utilization - survey

Utilization of localized and whole body imaging in patients with Neurofibromatosis type 1 for the evaluation of plexiform neurofibromas: Survey based assessment of Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS) members

Dear REiNS members,

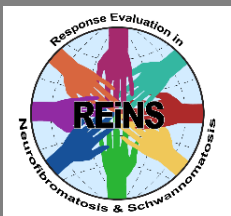
As members of the Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS) whole body-magnetic resonance (WB-MR) imaging committee, we are interested in the ways our community currently uses imaging (both localized and whole body) in routine clinical practice for the evaluation of plexiform neurofibromas. As such, we are reaching out to you to find out about the current practice patterns with respect to diagnostic imaging. Attached is an IRB exempt survey monkey poll (JHMI protocol# IRB00142837). Your participation is voluntary. Your completion of the survey or questionnaire will serve as your consent to be in this research study.

This is a short survey! (It took us 4 minutes 15 seconds). We would be grateful if you fill it out and we will share the results with everyone. We look forward to hearing from you.

Sincerely,

Shivani

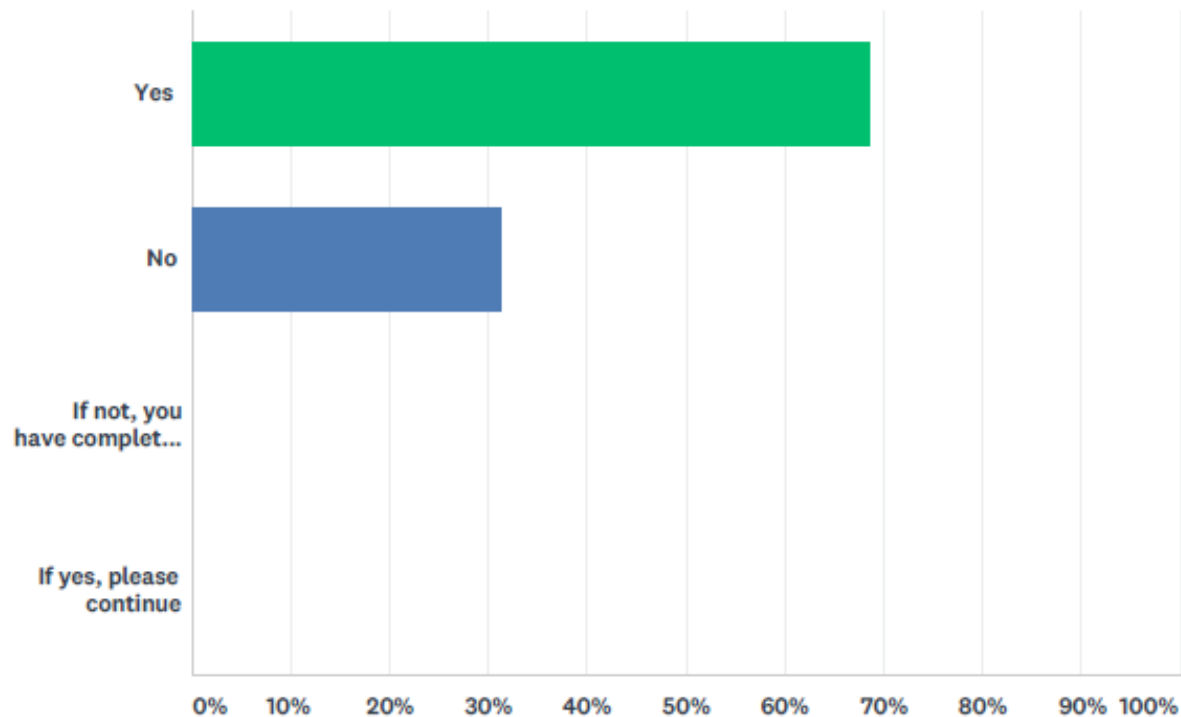
Shivani Ahlawat, MD
Assistant Professor,
Musculoskeletal Imaging Section
The Russell H. Morgan Department of Radiology & Radiological Science
The Johns Hopkins University School of Medicine



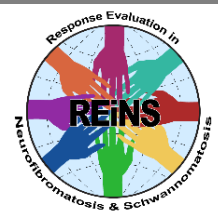
WB-MRI utilization

Q1 Are you the ordering clinician for imaging studies for people with NF1?

Answered: 35 Skipped: 0



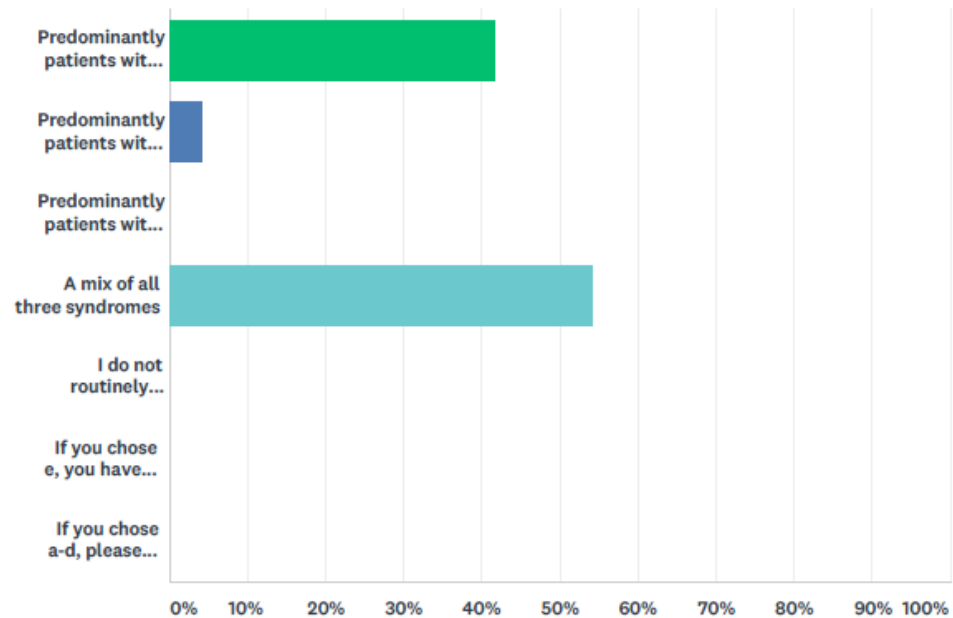
ANSWER CHOICES	RESPONSES	
Yes	68.57%	24
No	31.43%	11
If not, you have completed the survey	0.00%	0
If yes, please continue	0.00%	0
TOTAL		35



WB-MRI utilization

Q2 Which patient population do you see most often in your clinical practice?

Answered: 24 Skipped: 11



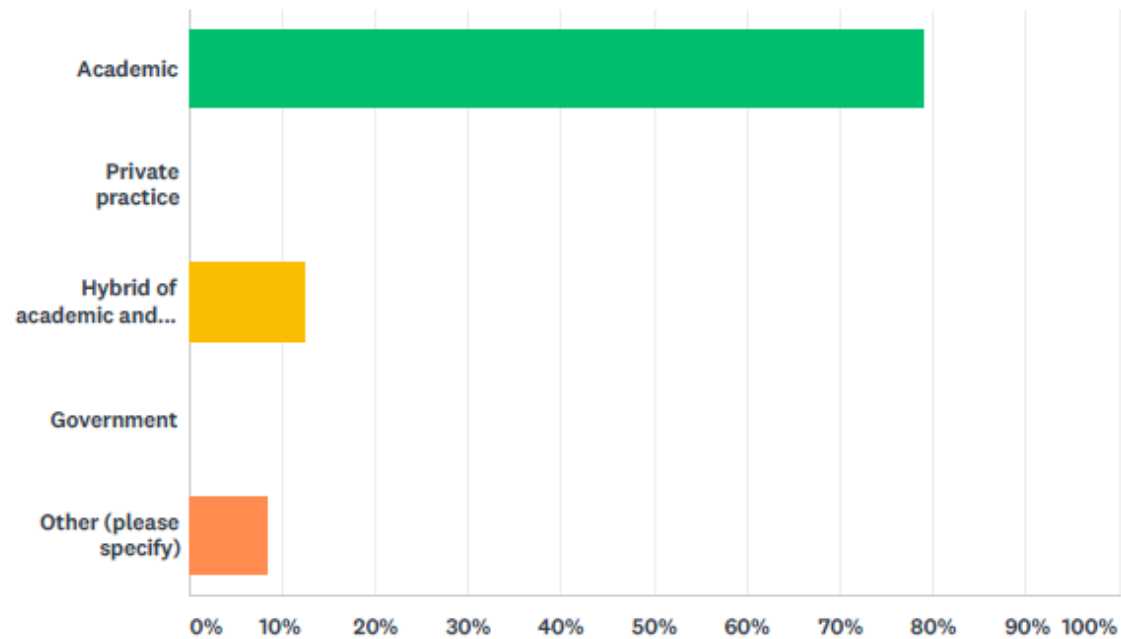
ANSWER CHOICES	RESPONSES
Predominantly patients with NF1	41.67% 10
Predominantly patients with NF2	4.17% 1
Predominantly patients with schwannomatosis	0.00% 0
A mix of all three syndromes	54.17% 13
I do not routinely provide care to patients with NF1, NF2 or schwannomatosis	0.00% 0
If you chose e, you have completed the survey	0.00% 0
If you chose a-d, please continue	0.00% 0
TOTAL	24



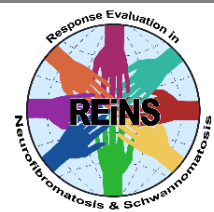
WB-MRI utilization

Q3 What best describes your clinical practice?

Answered: 24 Skipped: 11



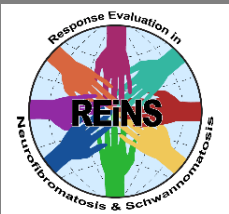
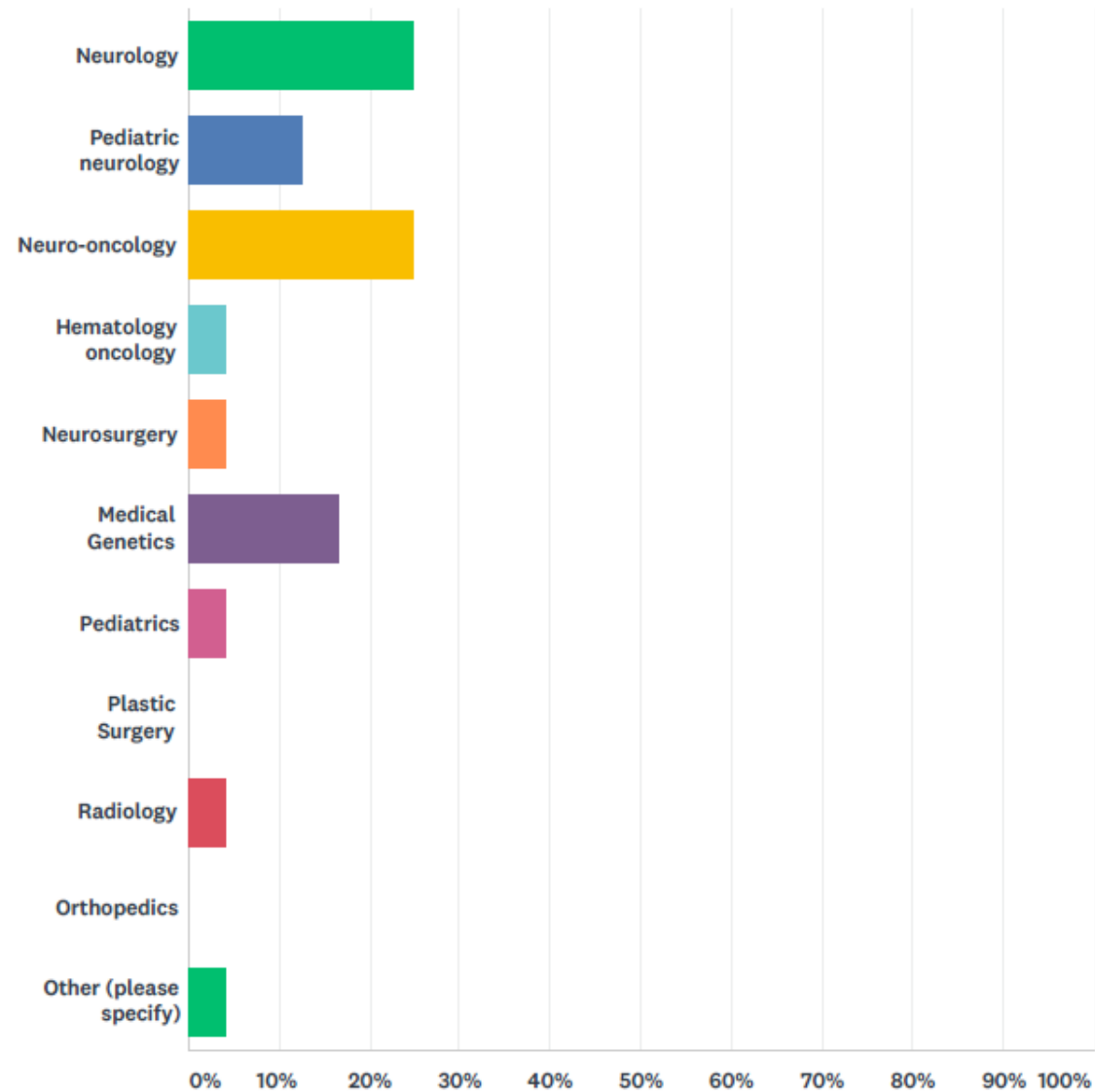
ANSWER CHOICES	RESPONSES	
Academic	79.17%	19
Private practice	0.00%	0
Hybrid of academic and private practice	12.50%	3
Government	0.00%	0
Other (please specify)	8.33%	2
TOTAL		24



WB-MRI utilization

Q4 What best describes your clinical field of expertise?

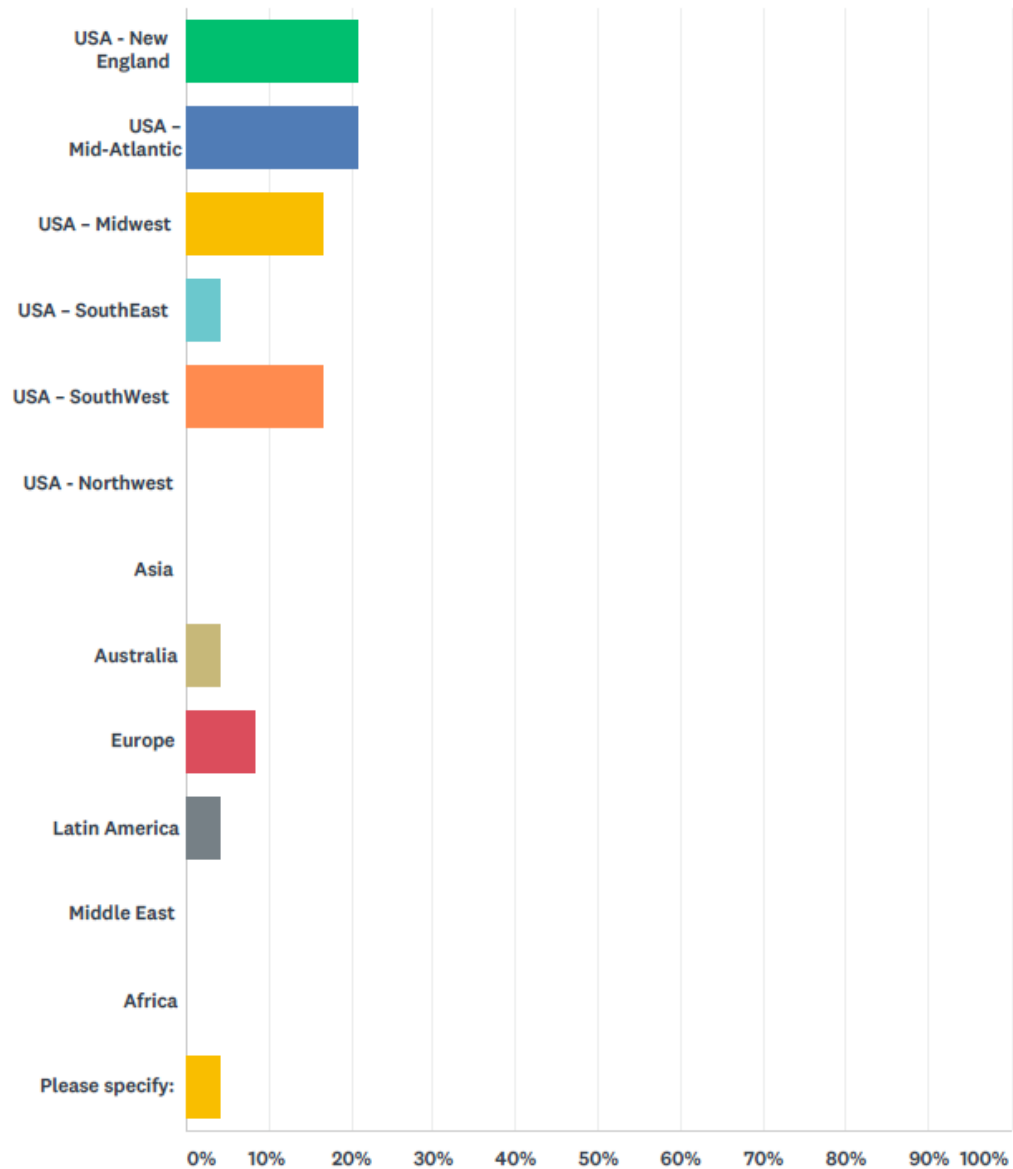
Answered: 24 Skipped: 11



WB-MRI utilization

Q5 Where is your clinical practice located?

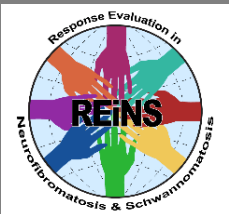
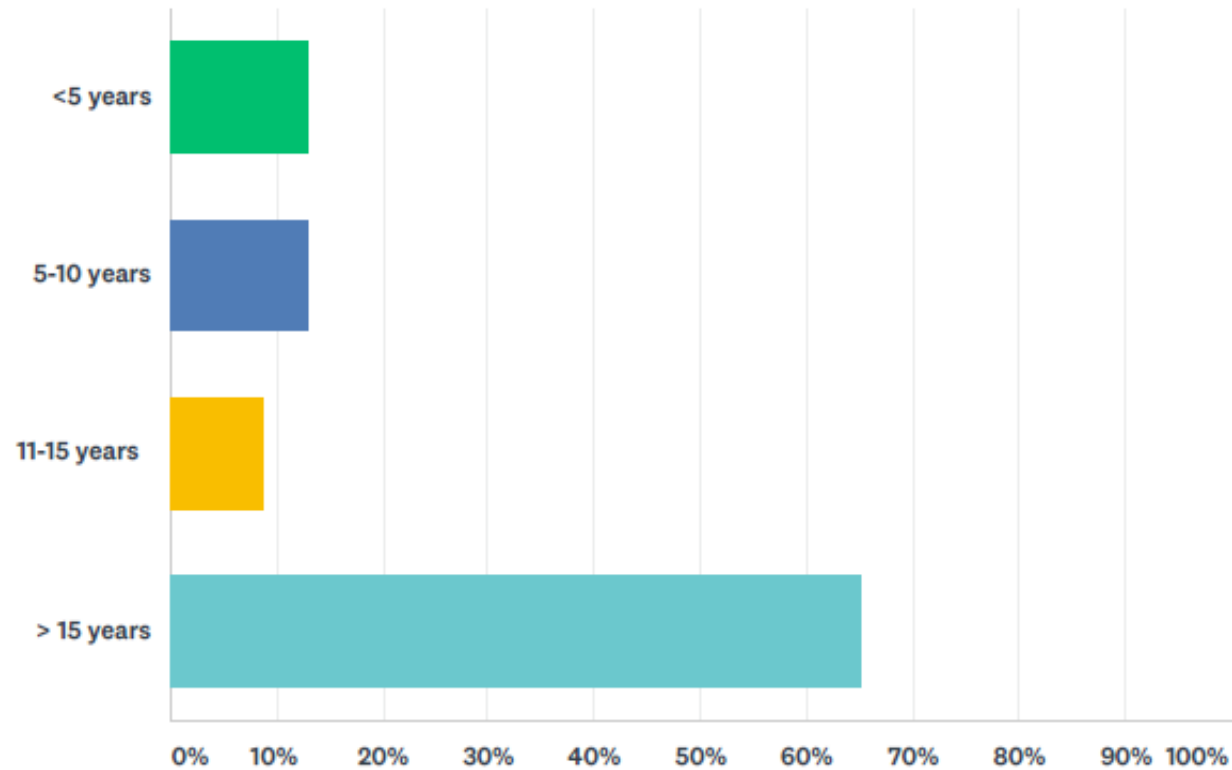
Answered: 24 Skipped: 11



WB-MRI utilization

Q6 How long has your practice focused on NF1 clinical care?

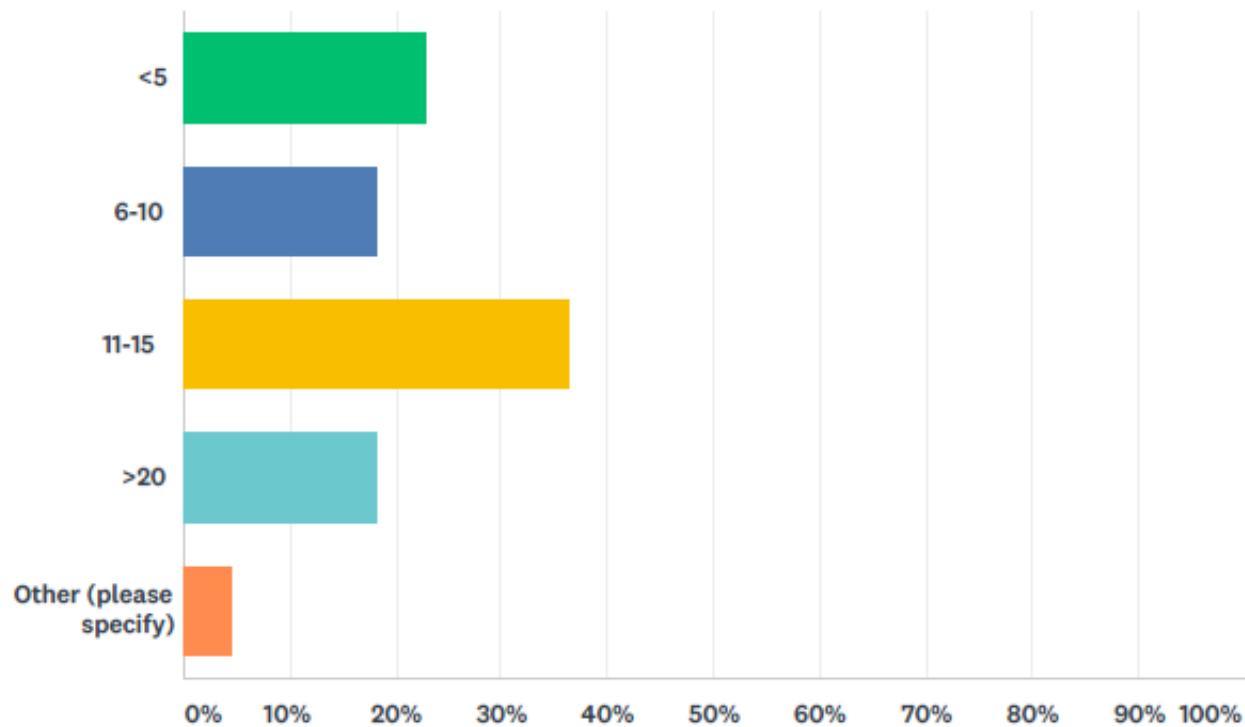
Answered: 23 Skipped: 12



WB-MRI utilization

Q7 How many patients with NF1 do you see in a typical work week?

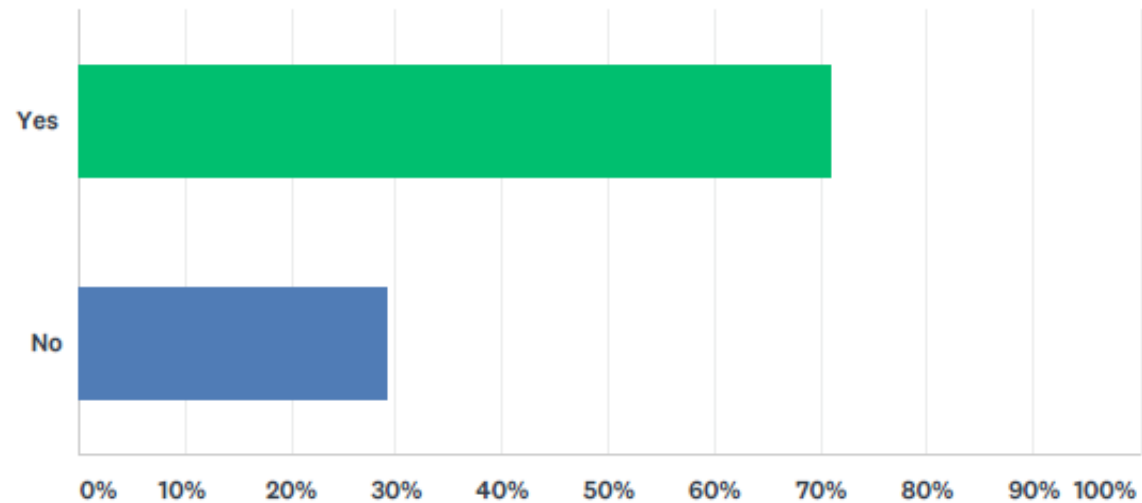
Answered: 22 Skipped: 13



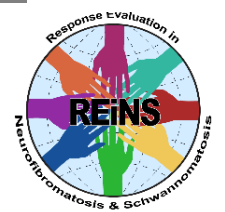
WB-MRI utilization

Q8 Do you have access to whole body MRI for your patients?

Answered: 24 Skipped: 11

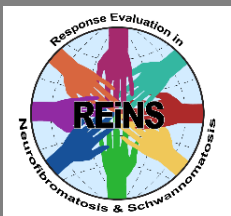


ANSWER CHOICES	RESPONSES	
Yes	70.83%	17
No	29.17%	7
TOTAL		24



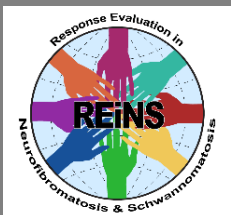
WB-MRI utilization

	Whole body Imaging Strategy	
Clinical scenario	WB-MRI	18F-FDG-PET/CT



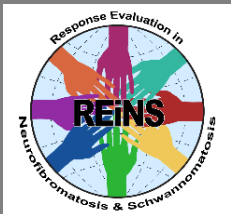
WB-MRI utilization

	Whole body Imaging Strategy	
Clinical scenario	WB-MRI	18F-FDG-PET/CT
Asymptomatic NF1 patient without known or visible plexiform PNST	21% (5/24)	0



WB-MRI utilization

	Whole body Imaging Strategy	
Clinical scenario	WB-MRI	18F-FDG-PET/CT
Asymptomatic NF1 patient without known or visible plexiform PNST	21% (5/24)	0
Asymptomatic NF1 patients with visible or known plexiform PNST	19% (4/21)	14% (3/21)



WB-MRI utilization

Clinical scenario	Whole body Imaging Strategy	
	WB-MRI	18F-FDG-PET/CT
Asymptomatic NF1 patient without known or visible plexiform PNST	21% (5/24)	0
Asymptomatic NF1 patients with visible or known plexiform PNST	19% (4/21)	14% (3/21)
Symptomatic NF1 patients without visible or known plexiform PNST	37% (7/19)	37% (7/19)



WB-MRI utilization

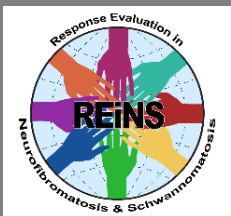
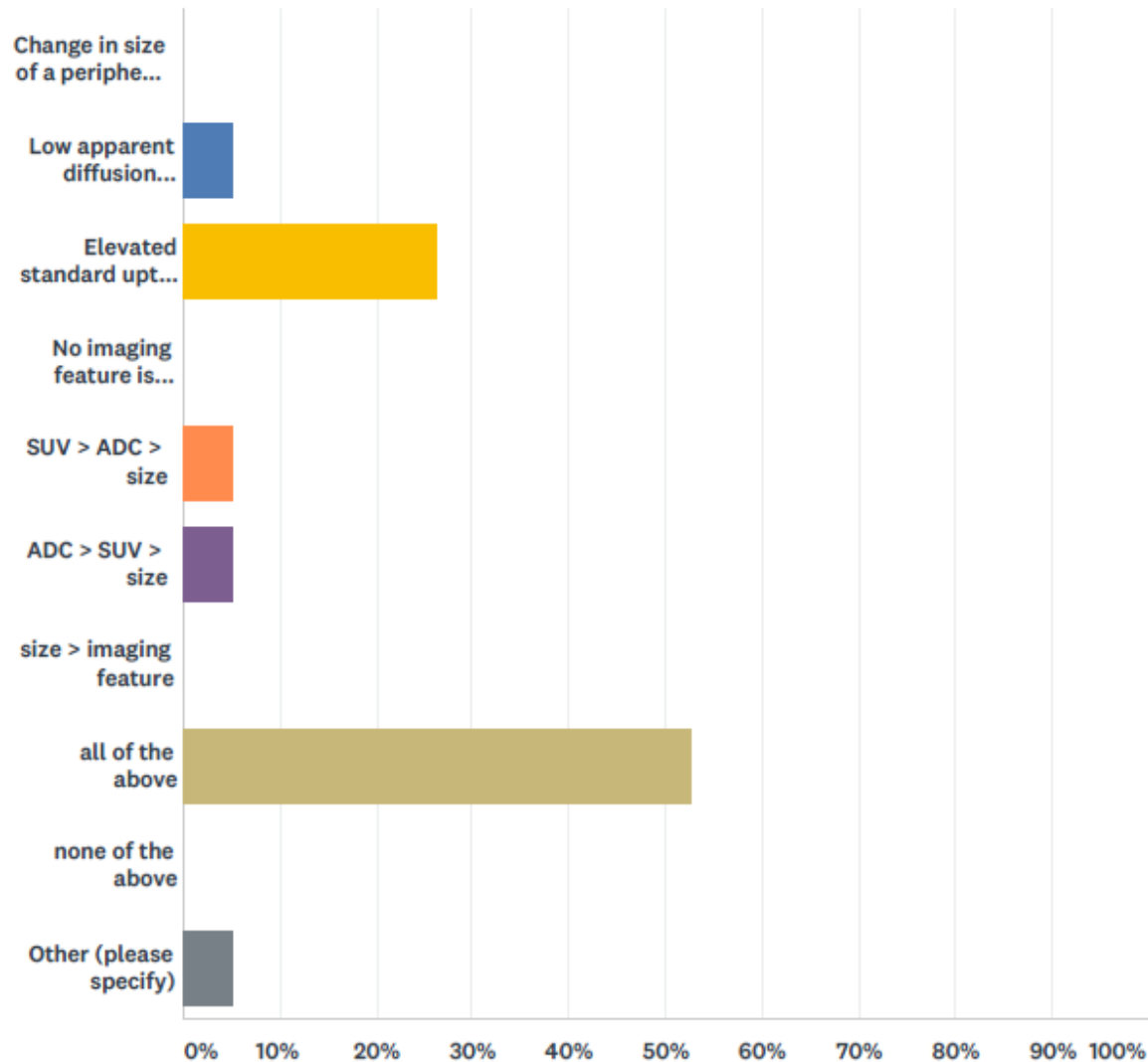
Clinical scenario	Whole body Imaging Strategy	
	WB-MRI	18F-FDG-PET/CT
Asymptomatic NF1 patient without known or visible plexiform PNST	21% (5/24)	0
Asymptomatic NF1 patients with visible or known plexiform PNST	19% (4/21)	14% (3/21)
Symptomatic NF1 patients without visible or known plexiform PNST	37% (7/19)	37% (7/19)
Symptomatic NF1 patients with visible or known plexiform PNST	37% (7/19)	84% (16/19)



WB-MRI utilization

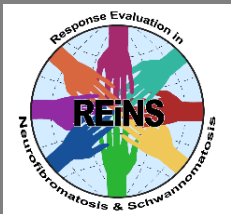
Q32 In your current clinical practice, which imaging feature is most helpful in deciding to proceed with biopsy?

Answered: 19 Skipped: 16



WB-MRI utilization

- Our survey results showed:
 - WB-MRI is not used a screening modality for asymptomatic patients by majority of the respondents.
 - In the survey, most common use tends to be symptomatic person with NF1 with or without known or visible plexiform neurofibroma.
 - Heterogeneity in the management strategy likely attributable to lack of an evidence-based consensus or guidelines for this patient population.



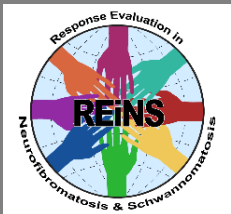
WB-MRI utilization

- Insurance coverage remains a barrier for obtaining WB-MRI at many centers.
 - Consider CTF/patient representative involvement for a billing code.
 - A billing code might increase access, particularly as a screening modality.



Whole Body Imaging

- *Prospective* evaluation of the two whole body imaging modalities will provide the necessary evidence to make robust recommendations for periodic surveillance in asymptomatic patients.



Conclusion

- Advances in WB-MRI acquisition with increasing inclusion of DWI/ADC mapping in imaging protocols across centers
- Prospective WB-MRI investigations needed, particularly with comparison of the two functional and metabolic whole body modalities

