Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

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Imaging Working Group Update

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Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

Imaging Working Group Projects

1. Detection and/or characterization of symptomatic peripheral lesions in people with NF2 and schwannomatosis (SWN)

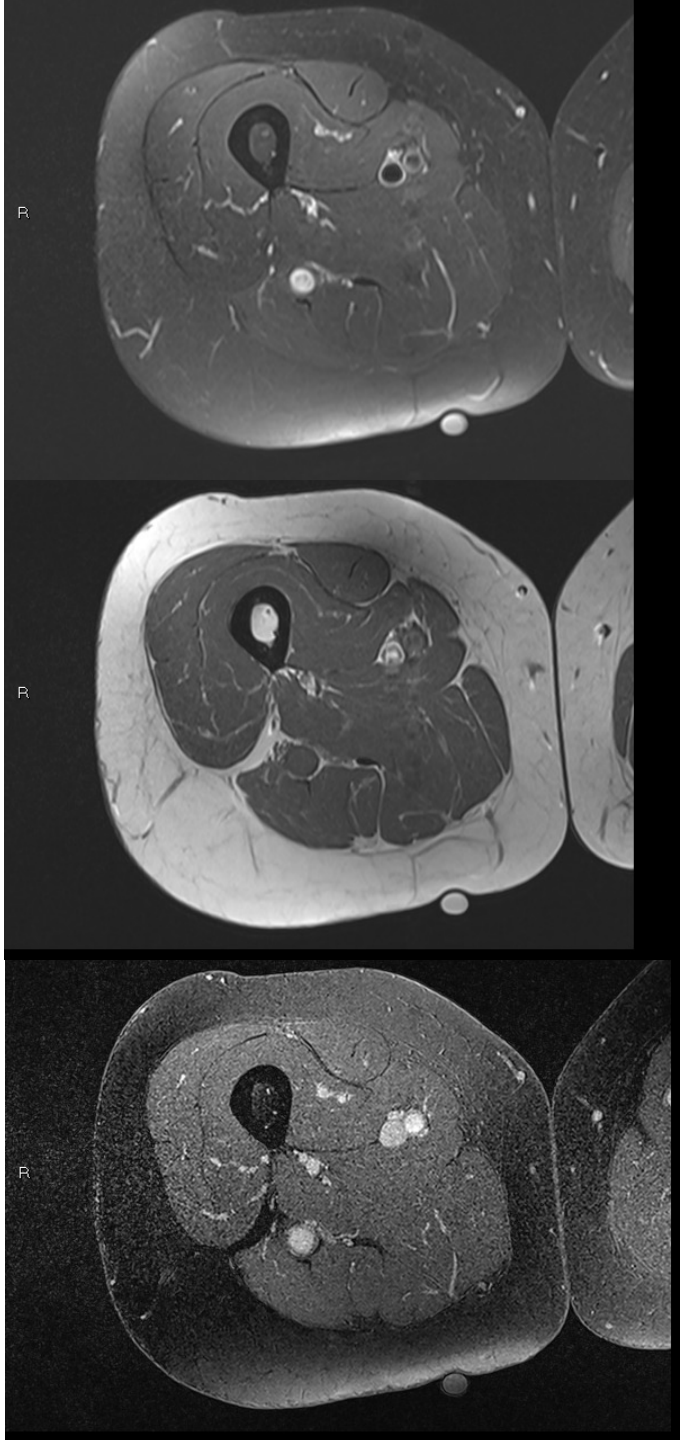
2. Assesment of the added value of IV contrast to a non-contrast MRI in the evaluation of plexiform neurofibromas for the detection of malignancy and operative planning

3. Treatment response criteria update

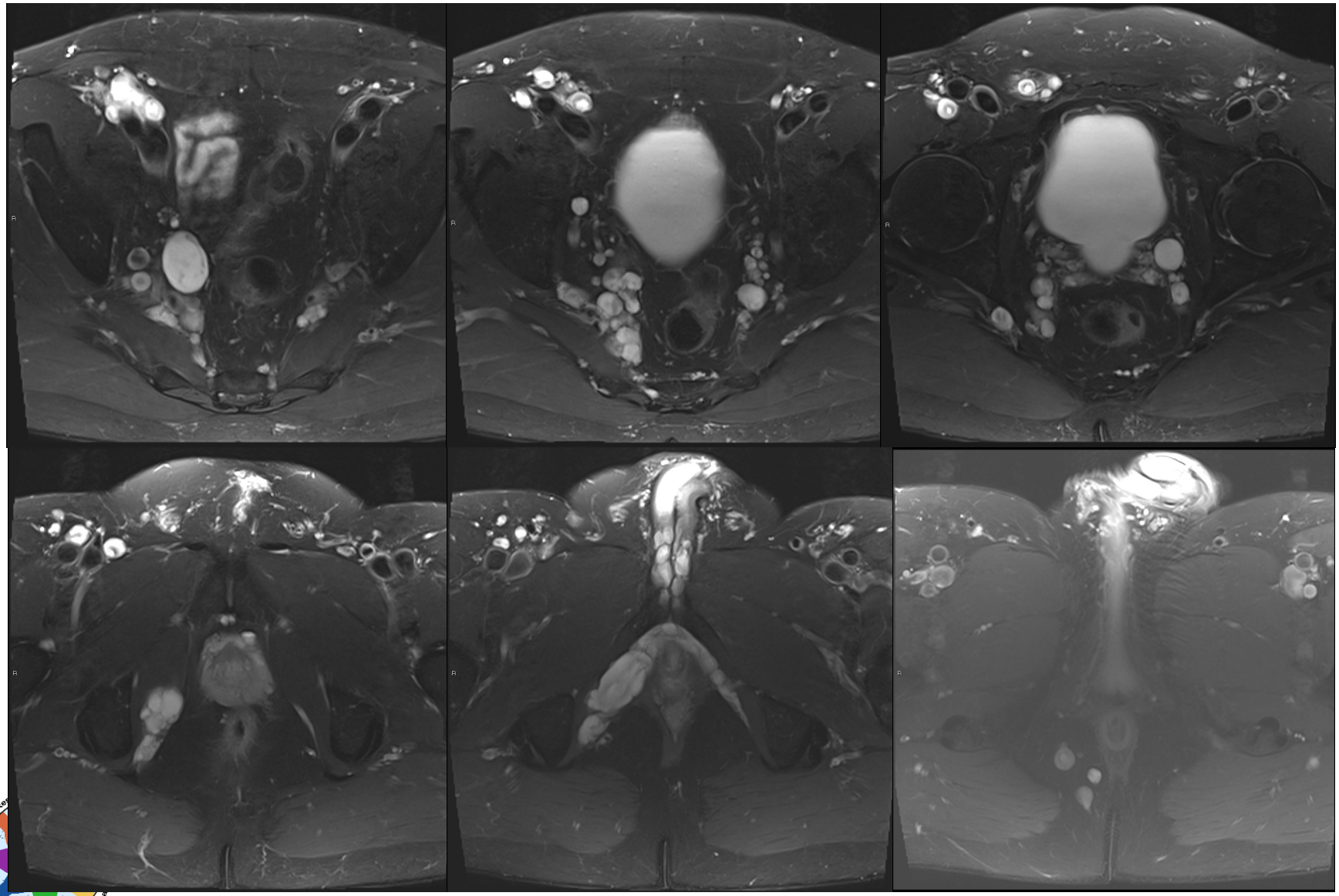
Detection and/or characterization of symptomatic peripheral lesions in people with NF2 and schwannomatosis (SWN)

Background

- Schwannoma is the hallmark tumor in both NF2 and schwannomatosis
- Management of peripheral lesions in NF2/SWN is symptom oriented
- Pain is MC symptom & challenging to treat
- Operative management reserved for symptomatic or rapidly growing lesions



Background



Background

- No clear relationship between pain intensity and
  - Tumor number
  - Size
  - Location
- Pain has both neuropathic and nociceptive features.
- No consensus approach for treating pain in these patients.

Plotkin SR, Wick A. Neurofibromatosis and Schwannomatosis. Semin Neurol. 2018 Feb;38(1):73-85.

Hypothesis

- Magnetic resonance imaging (MRI) can identify symptomatic lesions in people with NF2 and SWN.

Study Design

- Retrospective observational multi-center investigation comparing qualitative and quantitative MRI features of symptomatic peripheral lesions with asymptomatic lesions in people with NF2 and SWN

Study Design

- Eligibility criteria
  - Inclusion criteria:
    - Diagnosis of NF2/SWN +
    - WB-MRI or localized MRI with symptomatic and asymptomatic lesions in FOV
  - Exclusion criteria:
    - Non-diagnostic exam
    - Uncertainty regarding symptomatic lesion

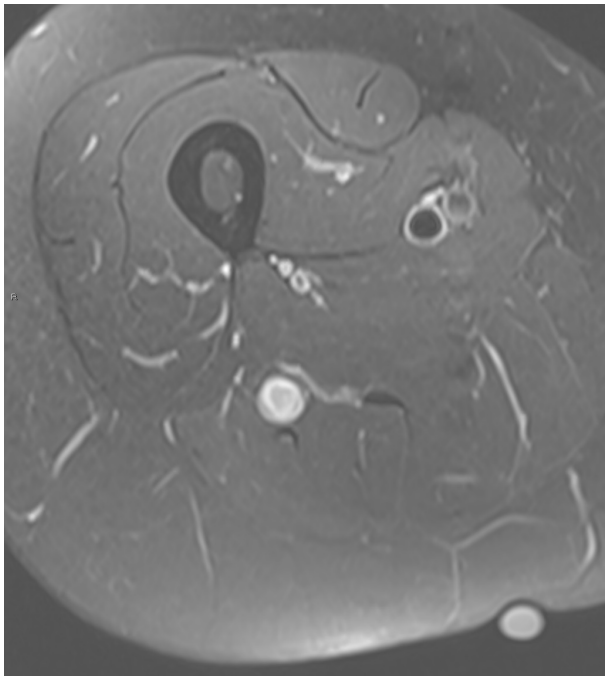
Study Design

- Reference criteria:
  - Clinical assessment and/or
  - Relief of pain/symptoms after operative management

Methods

For each symptomatic and asymptomatic peripheral lesion, radiologists with record:

- Size (AP, TV, CC)
- Signal intensity & heterogeneity on T1
- Signal intensity & heterogeneity on STIR/T2FS
- Enhancement/heterogeneity on T1+C
- Presence or absence of:
  - “Target” sign on STIR or T1+C
  - Perilesional edema
  - Perilesional enhancement
  - Internal cystic degeneration/necrosis
  - Skeletal muscle denervation
  - DWI characteristics if present



Study Objectives

- To compare the qualitative and quantitative MRI characteristics of symptomatic peripheral lesions with asymptomatic peripheral lesions in people with NF2 and SWN

Statistical Design

- Compare quantitative MRI features of symptomatic versus asymptomatic lesions
- Compare qualitative MRI features of symptomatic versus asymptomatic lesions
- Subanalyses in NF2 and SWN

Study Implementation

- Sites interested in participation:
  - University of Alabama
  - Johns Hopkins University
  - Mass General Hospital
  - Manchester University
  - Mayo Clinic

Added value of IV contrast to a non-contrast MRI in the evaluation of plexiform neurofibromas for the detection of malignancy and operative planning

Background

- Plexiform neurofibromas (PNs)
  - Histologically benign
  - Occur 50% of persons with neurofibromatosis type 1 (NF1)
  - Complications
    - Morbidity
    - Malignant transformation

Background

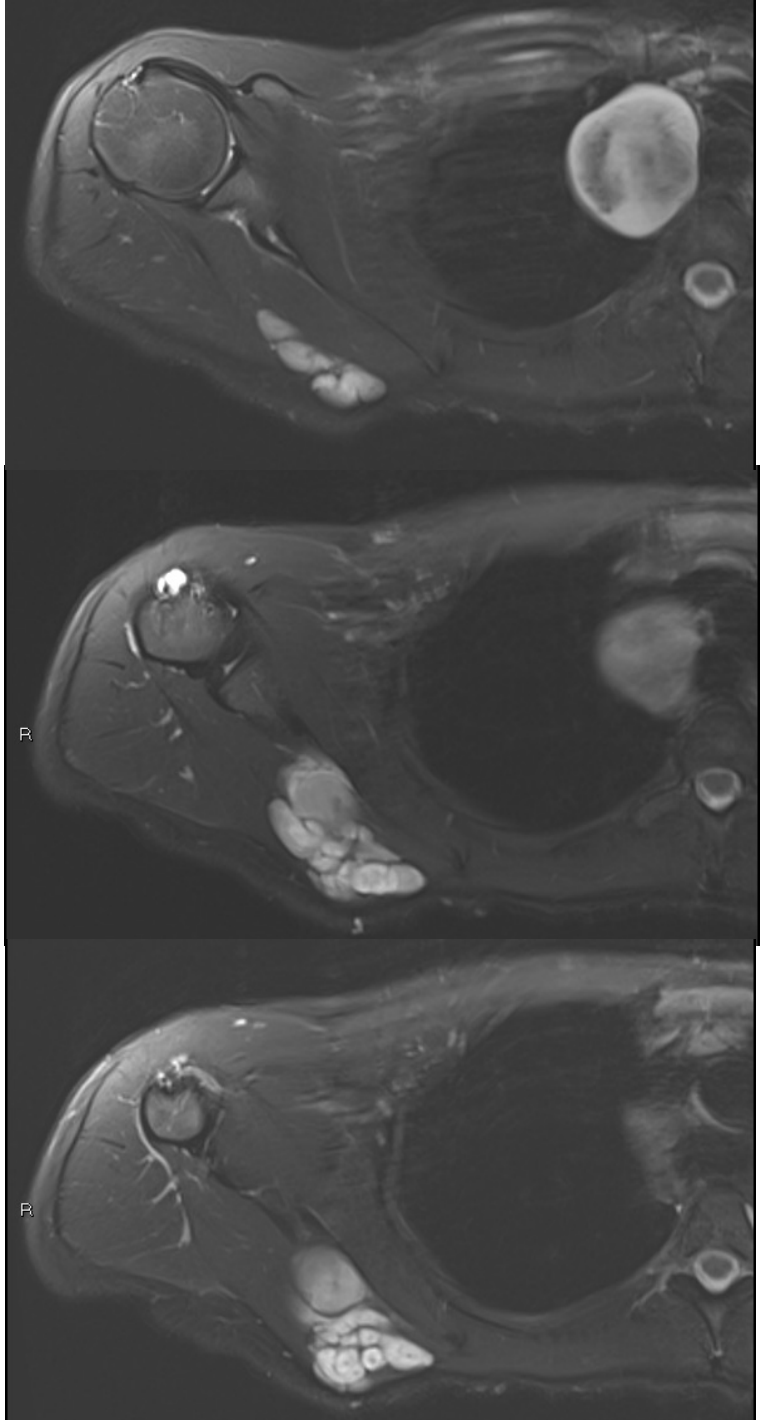
- Plexiform neurofibroma:
  - Detected clinically and/or via imaging (typically MRI)
    - Rarely biopsied
  - Monitored using MRI non-contrast STIR sequence
    - Volumetric analysis

Gross AM, Singh G, Akshintala S, Baldwin A, Dombi E, Ukwuani S, Goodwin A, Liewehr DJ, Steinberg SM, Widemann BC. Association of plexiform neurofibroma volume changes and development of clinical morbidities in neurofibromatosis 1. Neuro Oncol. 2018 Nov 12;20(12):1643-1651.

Background

- Non-contrast MRI using a high-quality STIR sequence alone is adequate for:
  - Detection of PN
  - Quantification of disease burden:
    - Volumetric analysis of PN
  - Longitudinal monitoring
  - Treatment response

- Gross AM, Wolters PL, Dombi E, Baldwin A, Whitcomb P, Fisher MJ, Weiss B, Kim A, Bornhorst M, Shah AC, Martin S, Roderick MC, Pichard DC, Carbonell A, Paul SM, Therrien J, Kapustina O, Heisey K, Clapp DW, Zhang C, Peer CJ, Figg WD, Smith M, Glod J, Blakeley JO, Steinberg SM, Venzon DJ, Doyle LA, Widemann BC. Selumetinib in Children with Inoperable Plexiform Neurofibromas. N Engl J Med. 2020 Apr 9;382(15):1430-1442.
- Gross AM, Singh G, Akshintala S, Baldwin A, Dombi E, Ukwuani S, Goodwin A, Liewehr DJ, Steinberg SM, Widemann BC. Association of plexiform neurofibroma volume changes and development of clinical morbidities in neurofibromatosis 1. Neuro Oncol. 2018 Nov 12;20(12):1643-1651.
- Cai W, Steinberg SM, Bredella MA, Basinsky G, Somarouthu B, Plotkin SR, Solomon J, Widemann BC, Harris GJ, Dombi E. Volumetric MRI Analysis of Plexiform Neurofibromas in Neurofibromatosis Type 1: Comparison of Two Methods. Acad Radiol. 2018 Feb;25(2):144-152.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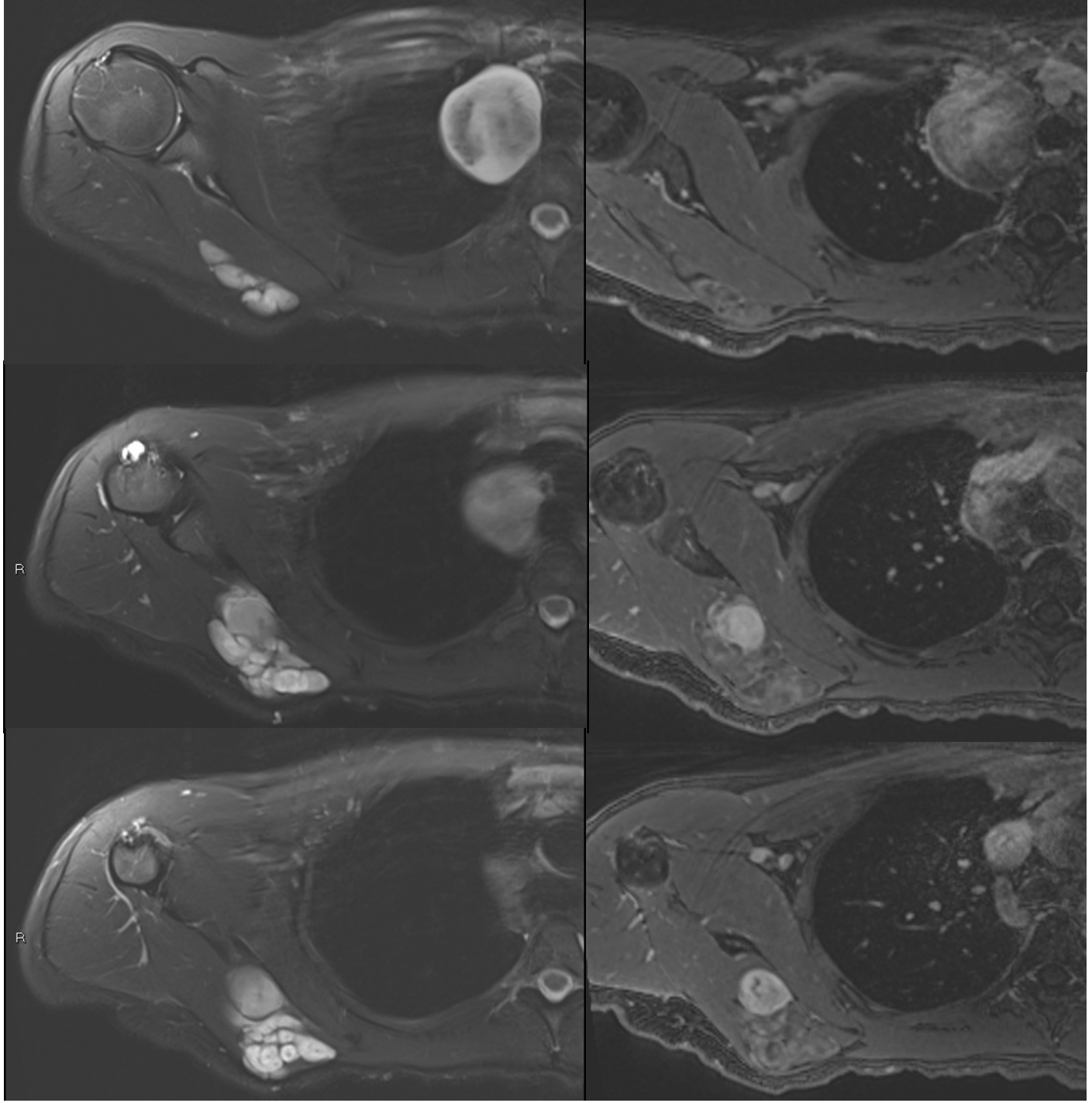
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Hypothesis

- Contrast-enhanced MRI sequences maybe helpful in the detection of malignant transformation in the background of PN
- Contrast-enhanced MRI sequences maybe helpful for the assessment of anatomic extent if operative management is planned

Study Design

- Retrospective observational multi-center investigation comparing non-contrast MRI sequences (STIR) to contrast-enhanced MRI sequences for
  1. Detection of malignant transformation
  2. Operative planning

Study Design

Eligibility criteria

- Inclusion criteria:
  - Diagnosis of NF1+
  - WB-MRI or localized MRI with Plexiform neurofibroma
    - Enrich for spine/brachial plexus where DWI fails
  - PN – MPNST (?Atypical/ANNUBP)
  - PN + MPNST (?Atypical/ANNUBP)

- Exclusion criteria:
  - Non-diagnostic exam
  - No contrast enhanced sequences
  - Uncertainty regarding diagnosis

Study Design

- Reference criteria:
  - STIR appearance of plexiform neurofibroma (majority are not path proven) and clinical stability or histology for absence of MPNST
  - +/- histology if available
  - Histology for MPNST

Methods

- Evaluate imaging in 2 sessions independently:
  - Session 1 – STIR only
  - Session 2 – STIR + contrast enhanced sequences

Methods: Malignant transformation

For each session, radiologists will record:

- Imaging features:
  - Session 1
    - Size (AP, TV, CC)
    - Signal intensity & heterogeneity on T1
    - Signal intensity & heterogeneity on STIR/T2FS
    - “Target” sign on STIR
    - Skeletal muscle denervation
    - DWI characteristics if present
  - Session 2
    - Enhancement/heterogeneity on T1+C
    - “Target” sign on T1+C
    - Perilesional edema/enhancement
    - Internal cystic degeneration/necrosis
  - Diagnostic confidence (for session 1 and session 2):
    - PN only (no suspicion of malignant transformation)
    - PN with low suspicion of malignant transformation
    - PN with high suspicion of malignant transformation
    - PN with definite malignant transformation

Methods: PN surgical planning

For each session, radiologists + surgeons will record:

- Anatomic extent of PN (session 1 and session 2):
  - Skin/subcutaneous involvement
  - Extra-compartmental extension
  - Intra-osseous extension
  - Intra-articular extension
  - Vascularity

- Diagnostic confidence (after both sessions):
  - STIR alone adequate (contrast enhanced sequences were not necessary)
  - Contrast enhanced sequences were mildly useful
  - Contrast enhanced sequences were moderately useful
  - Contrast enhanced sequences were necessary

Study Objectives

- To evaluate the added value of intravenous contrast material to non-contrast MRI sequences (STIR) for
  - Detection of malignant transformation in the setting of a PN
  - For evaluation of anatomic assessment if operative management is required

Statistical Design

- Compare session 1 and session 2
  - Accuracy/diagnostic confidence for the detection of malignant transformation in the setting of a PN
  - Diagnostic confidence regarding anatomic assessment if operative management is required

Study Implementation

- Sites interested in participation:
  - University of Alabama
  - Johns Hopkins University
  - Mass General Hospital
  - Manchester University
  - Mayo Clinic
  - Children's Hospital of Philadelphia

Feedback from REiNS community

- Central storage and data transfer versus image sharing anonymously via zoom/teams
- Interested radiologists willing to interpret images
- Interested surgeons who operate on PNs willing to participate

Thank you

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