

Response Evaluation In Neurofibromatosis Schwannomatosis  
INTERNATIONAL COLLABORATION

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# REiNS Functional Group Update

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Response Evaluation In Neurofibromatosis Schwannomatosis  
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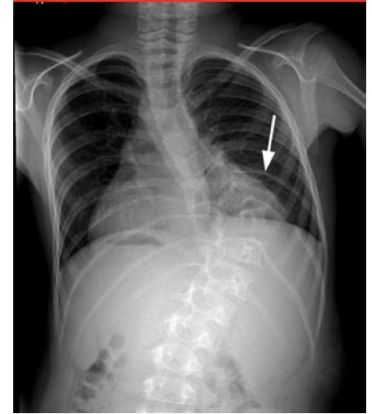
# Functional Group Update

- Focus on skeletal manifestations in NF1 including:
  - Scoliosis
    - With and without paraspinal neurofibroma
  - Osteopenia
    - Systemic and localized
  - Dysplasia/Pseudoarthrosis
- Skeletal outcomes reviewed in March 2021 meeting



# Scoliosis in NF1: X-Ray vs MRI

- Standing Radiograph (X-Ray) is the gold standard for measuring scoliosis angle
- Magnetic Resonance Imaging (MRI):
  - Standard imaging modality for NF related tumors
  - Can visualize progression of scoliosis on MRI
  - Uncertain relationship between scoliosis curve measured on radiograph vs MRI



AP radiograph demonstrating rib penciling (arrow) in a patient with neurofibromatosis-1. (Courtesy of Lori A. Karol, MD, Texas Scottish Rite Hospital, Dallas, TX.)

04-2003

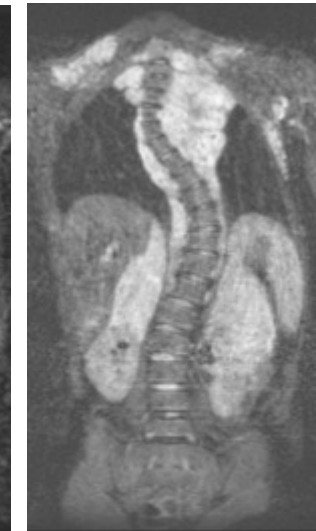
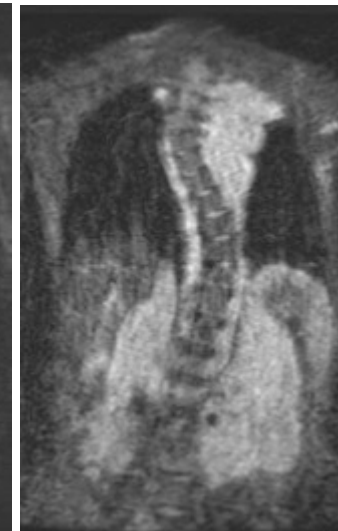
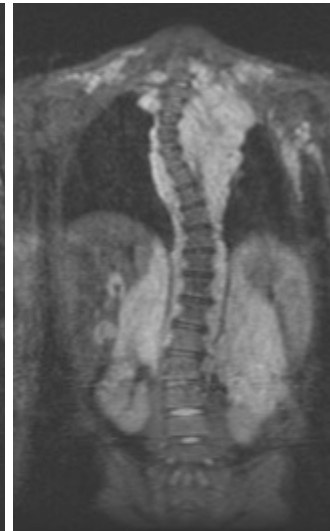
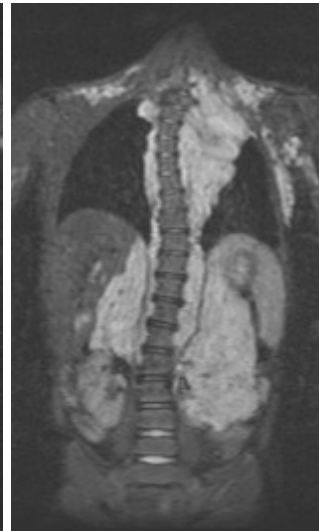
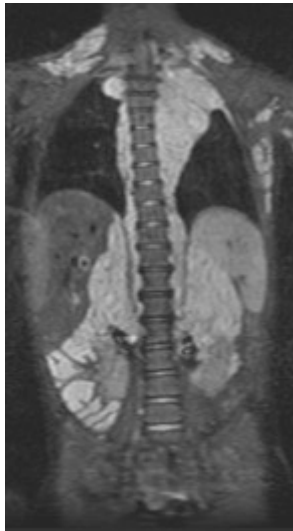
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04-2006

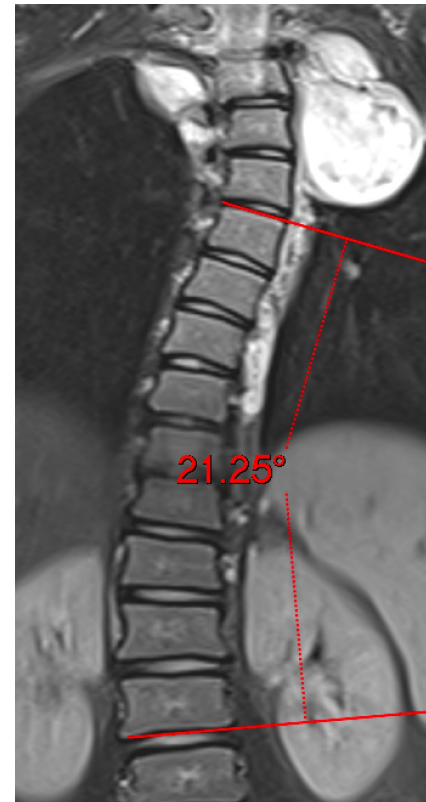
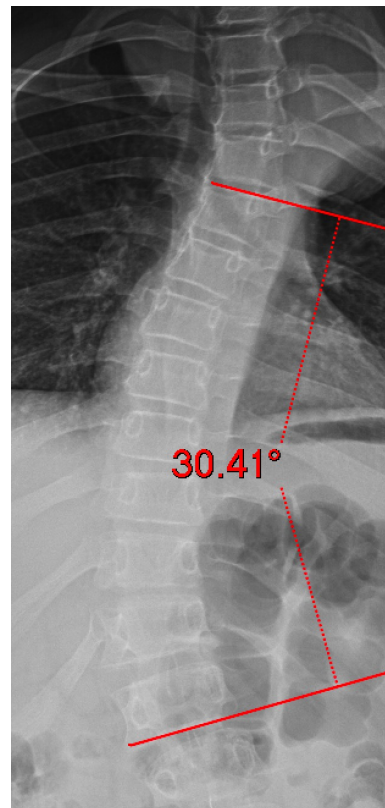
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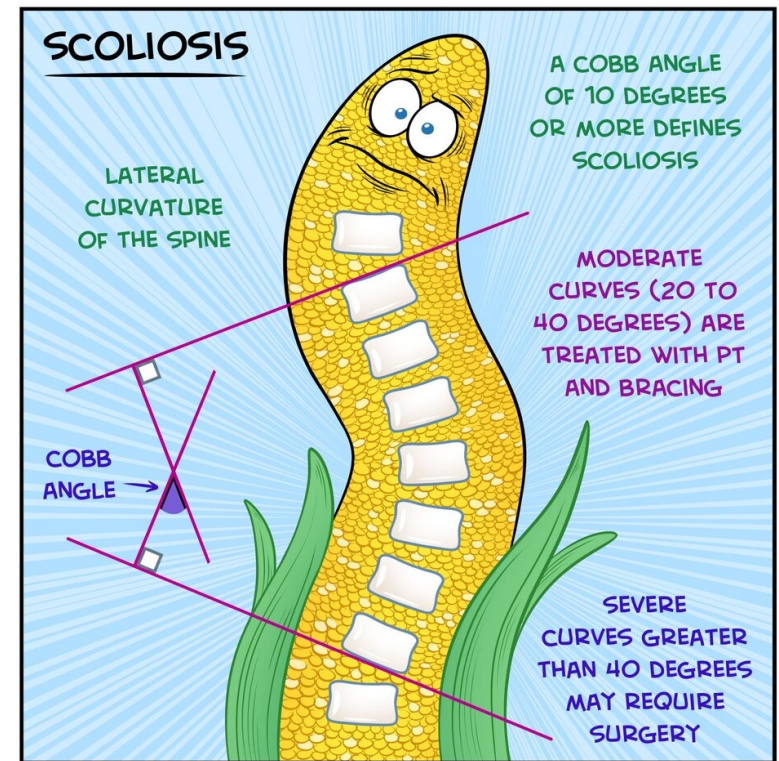
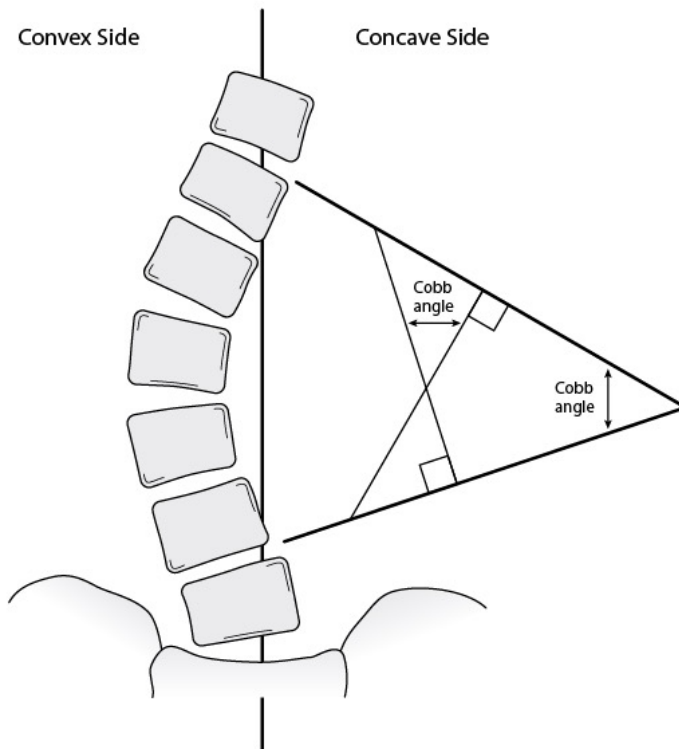
# Hypotheses

The degree of spinal curvature visualized on MRI can be directly correlated with the degree of spinal curvature seen in standard standing scoliosis radiographs (Cobb angle) obtained at the same time point



# Hypotheses

Changes in spinal curvature over time can be appreciated on MRI and correlate directly with the change in spinal curvature seen in standard standing scoliosis radiographs obtained at the same time points.



# Study Design & Eligibility

- Design: Retrospective review comparing Cobb angles of MRI scans and standing radiographs of the spine obtained on patients as part of clinical care or a previous clinical trial.
- Eligibility: Patients (any age) with a clinical or genetic diagnosis of NF1 who have an MRI which includes the entire spine (cervical, thoracic and lumbar) and standing scoliosis radiographs completed within 3 months of each other



# Scoliosis Study Implementation

- Independent Radiologist Readers identified
  - Dr. Connie Chang, MGH
  - Dr. Viral Jain, Cincinnati Children's
  - Dr. Miriam Bredella, MGH (Tie-Breaker)
- Feedback from REiNS Community (March 2021 Meeting)
- Identify sites for involvement:
  - NIH, Boston Children's, Massachusetts General Hospital, Cincinnati Children's, Manchester University
- Write protocol & submit for IRB approval
- Collect + deidentify eligible scans and calculate MRI and radiograph Cobb angles





# Recommended Endpoints for Scoliosis and Osteoporosis in NF1

- Committee plans to write a paper including:
  - Overview of available techniques
  - Consensus recommendations regarding which measurements should be used in future trials
- Combined paper for scoliosis and osteoporosis vs two separate papers



# Recommended Endpoints for Scoliosis and Osteoporosis in NF1

- Need for consensus recommendation given possible impact of new systemic treatments on skeletal manifestations (e.g. MEK inhibitor)
- Challenges Remaining for Developing Consensus Recommendations:
  - Need additional input from experts in the field (e.g. radiologist specializing in DEXA scans, endocrinologist specializing in bone health)
  - Definition of clinically meaningful changes in NF1 subjects to be determined

