

Response Evaluation In Neurofibromatosis Schwannomatosis INTERNATIONAL COLLABORATION

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Getting Ahead of the Curve: MRI vs Radiographs for NF1 Related Scoliosis

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Response Evaluation In Neurofibromatosis Schwannomatosis
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Background

- Scoliosis occurs in 10-49% of patients with NF1
 - Non-Dystrophic
 - Dystrophic
- Curvature measured using Cobb angle
- Standing radiographs (X-rays) gold standard for measurement of scoliosis
 - Pros:
 - Standard measurement of scoliosis for clinical management
 - Standing films account for impact of gravity on curvature
 - Cons:
 - Radiation exposure (minimal)
 - May not have been done on clinical trial or natural history patients



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



Background (continued)

- 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

04-2003

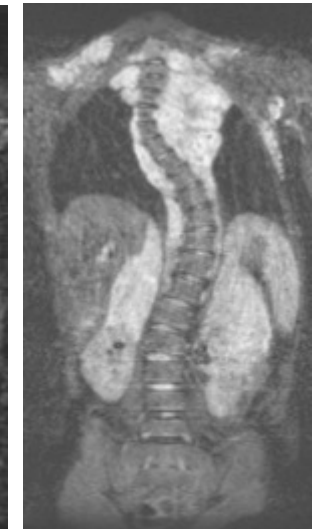
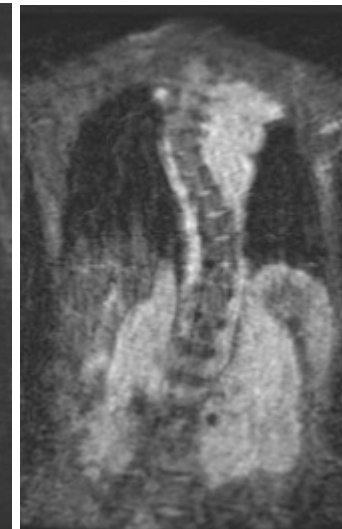
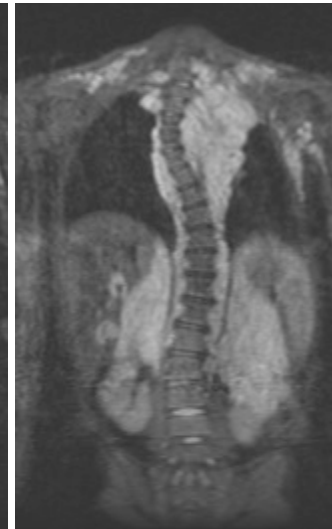
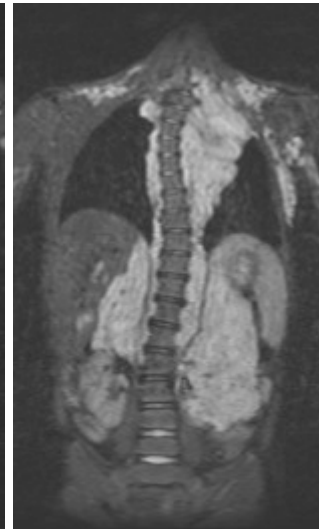
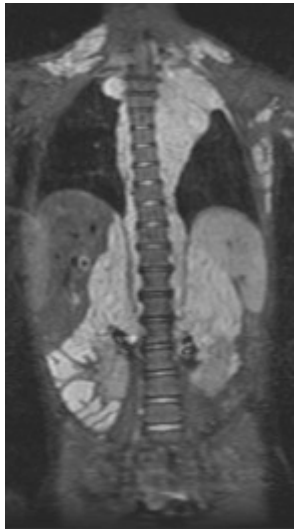
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Background

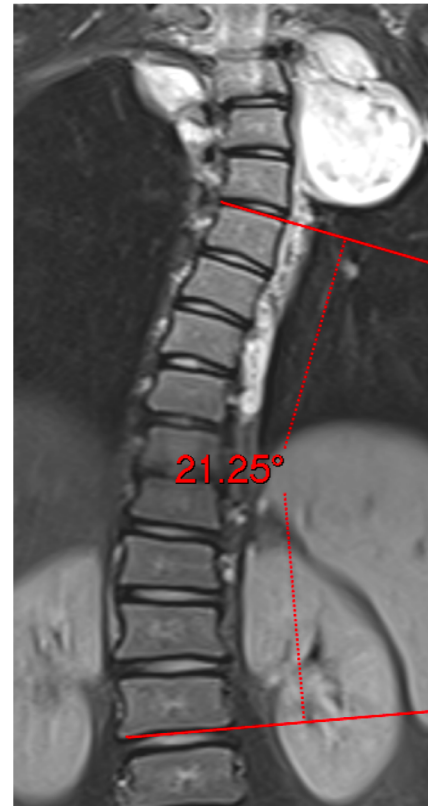
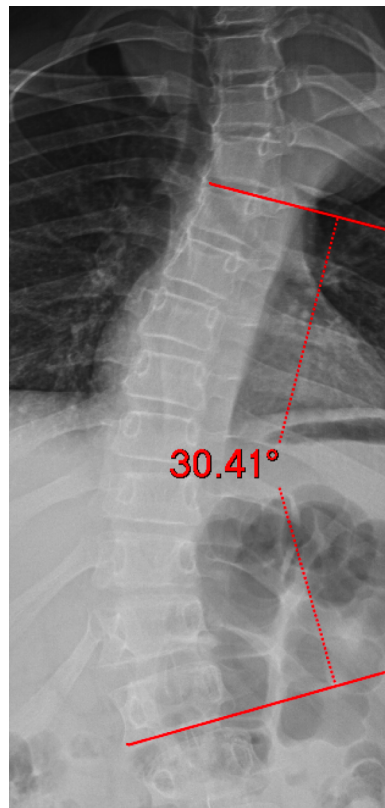
- Ghandari et al, 2020
 - Compared MRI and standing radiographs on 103 patients with idiopathic scoliosis
 - Results:
 - Direct correlation between cobb angle on MRI and cobb angle on plain radiograph
 - In their study:
 - Mean \pm SD difference (X-Ray Cobb Angle – MRI Cobb Angle) was $11 \pm 1.4^\circ$
 - Direct correlation between MRI and X-ray Cobb angles:

$$\text{MRI Cobb Angle} = 0.9^* (\text{XRAY Cobb Angle}) - 5.31$$



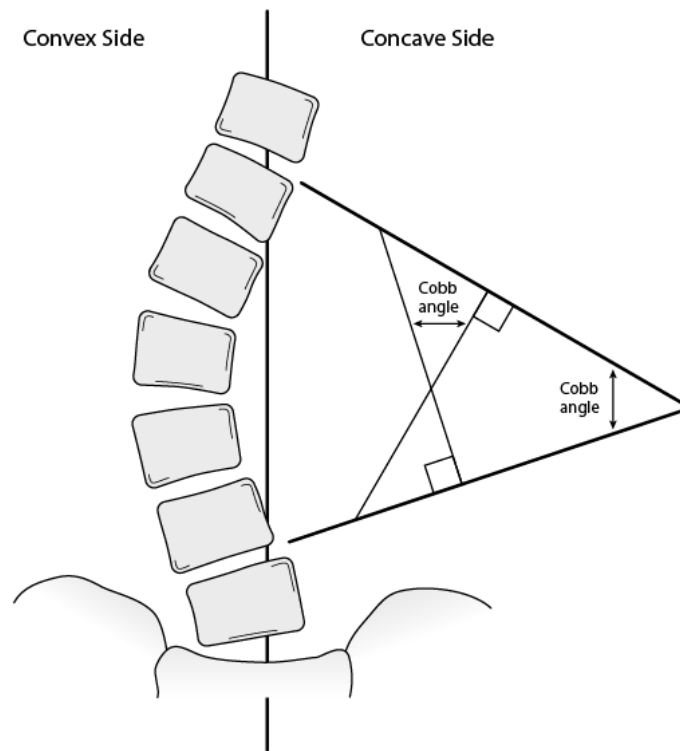
Hypotheses

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.



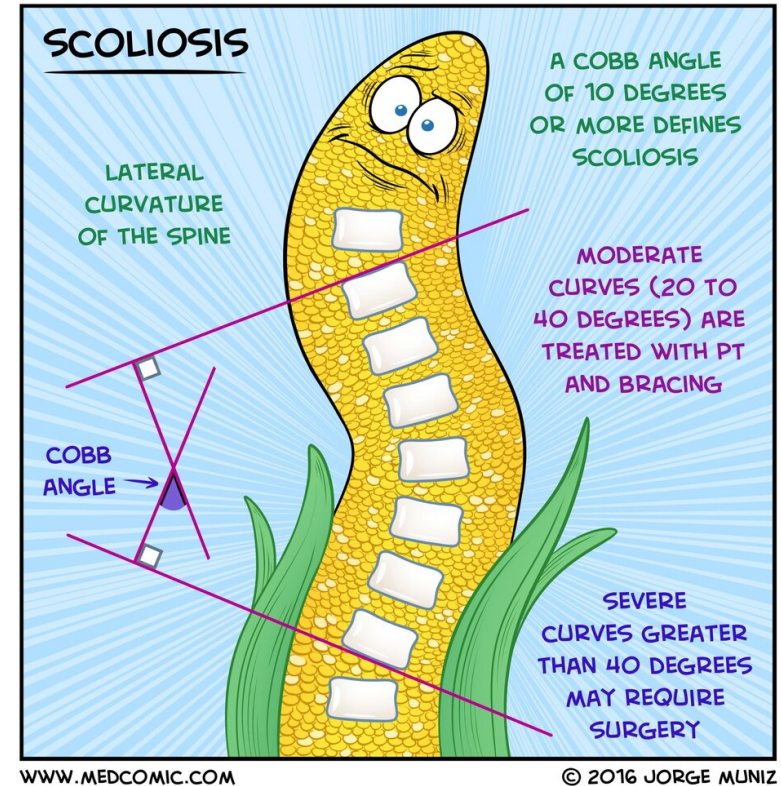
Study Design & Eligibility

- Design: Retrospective review comparing 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



Methods

- For each MRI /Radiograph Pair:
 - 2 Independent radiologists will calculate the Cobb angle for each scan
 - The first rater will assign bony landmarks/levels used to complete the measurement.
 - If the measurements are within 5 degrees of each other, the angle from the more senior rater will be used
 - If the measures are >5 degrees apart, a 3rd rater will be used as a tie-breaker



Study Objectives

- Primary Objective:

- To determine if there is a correlation between the MRI and X-ray Cobb angles in the NF1 population

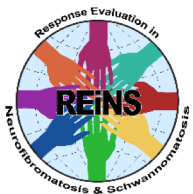
- Secondary Objectives:

1. To investigate if the changes over time in the Cobb angle as measured by standing X-ray and by MRI taken at matching consecutive time points agree with one another
2. To estimate the degree to which the Cobb angles measured from standing X-ray and from MRIs obtained from the same patient within 3 months of each other are similar

Study Objectives

- Exploratory Objectives:

1. To determine the degree to which our results are consistent with formula presented in Ghandari et al ($MRI = 0.9(Xray) - 5.31$)
2. To see if MRI can be used to detect features of dystrophic scoliosis that are consistent with those found on standing X-ray
3. To see if the presence or absence of other spinal abnormalities (e.g. kyphosis) can be equally appreciated on both MRI and standing X-ray obtained within 3 months of each other



Statistical Design & Sample Size

- **Sample Size:** 50 Subjects
- **Primary Endpoint:**
 - Spearman or Pearson Correlation of MRI vs Radiograph Cobb Angle obtained within 3 months of each other
 - With 50 patients: A one-sided 95% confidence interval for $r=0.90$ will have a lower limit of 0.84



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

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

