Neurofibromatosis type 1 with Dystrophic Scoliosis: A Multicenter Inter-observer Reliability Study of Radiographic Characteristics

Ledonio, Charles Gerald T.[1]; Polly, David W.[1]; Brearley, Ann M.[1]; Crawford, Alvin H.[2]; Sucato, Daniel J.[3]; Carreon, Leah Y.[4]; Larson, A. Noelle[5]; Stevenson, David A.[6]; Vitale, Michael G.[7]; Moertel, Christopher L.[1]

1. University of MInnesota, Minneapolis, MN, United States.
2. Cincinnati Children's Hospital, Cincinnati, OH, United States.
3. Texas Scottish Rite Hospital for Children, Dallas, TX, United States.
4. Norton Leatherman Spine Center, Louisville, KY, United States.
5. Mayo Clinic, Rochester, MN, United States.
6. University of Utah, Salt Lake City, UT, United States.
7. Columbia University Medical Center, New York, NY, United States.

Disclosure

• Presenter: Charles T. Ledonio, MD	(a) SRS, POSNA, SRF, OREF, DOD
• Co-Authors:	
– David W. Polly, Jr., MD	(a) SRS, POSNA, SRF, OREF, DOD (b) Medtronic Spine & Navigation ended 10/1/09 & 6/28/10
– Ann M. Brearley, PhD	No relationship
– Alvin H. Crawford, MD	(a) OREF (b) Unpaid consultant DePuy
– Daniel J. Sucato, MD	No relationship
– Leah Y. Carreon, MD	(a) Norton healthcare (e) Norton, OREF, NIH
– A. Noelle Larson, MD	(a) OREF
– David A. Stevenson, MD	No relationship
– Michael G. Vitale, MD	(a) AO Spine/Synthes, Biomet, CWSDRF, Medtronic, OREF (b) Biomet, CWSDSG, Stryker (e) Biomet, CWSDSG, FOXPSDSG, Medtronic
– Christopher L. Moertel, MD	No relationship

This study was funded by a research grant from:
DOD Neurofibromatosis Investigator-Initiated Research Award (# W81XWH-10-1-0469)

a. Grants/Research Support
b. Consultant
c. Stock/Shareholder
d. Speakers' Bureau
e. Other Financial Support

Scoliosis in Neurofibromatosis type1: Dystrophic or non-dystrophic

- Nondystrophic and dystrophic
- Most common osseous defect
- 2% of pts with scoliosis will have NF-1
- 30% of patients with NF-1 have spine disorders
- Dystrophic more severe

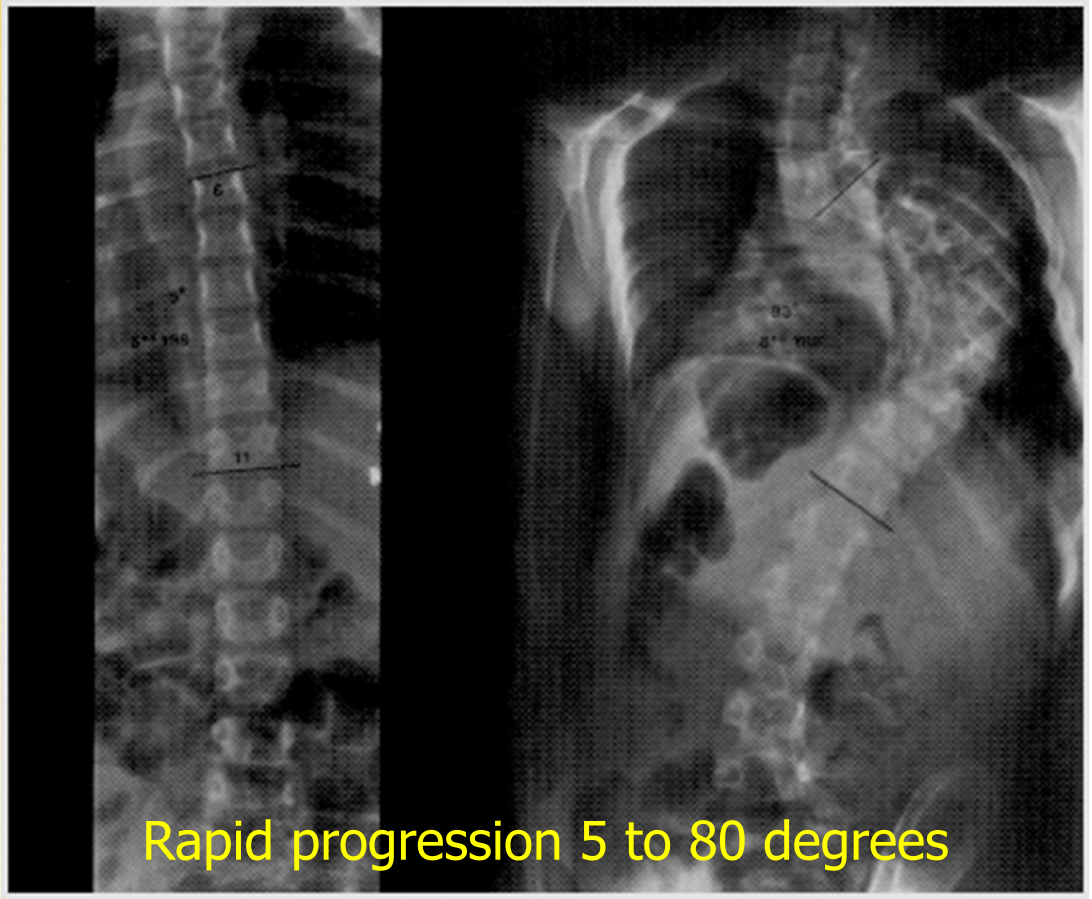
Crawford OCNA 2007

Table 1. Prevalence of scoliosis in NF1

	Scoliosis Prevalence	Dystrophic	Non-Dystrophic
McCarroll (1950)	41%		
Hunt & Pugh (1961)	14.6%	30%	5.0 %
Lewis & Pallios (1963)	39%		
Scott (1965)	12-20%		
Chaglessian (1976)	26%		
Held (1979)	36%		
Crawford (1986)	64%		
DeSimone (1988)	53%		
Sirais & Brennan (1990)	69%		
Akbarnia (1992)	10%	61%	39%

Natural History

- *Calvert et al, JBJS Br 1989*
  - Treated (n=34) and untreated (n=32) w/ NF1 scoliosis
  - 75% untreated group had kyphoscoliosis
  - Severe anterior scalloping – progressed 23˚ /yr
  - All others 7˚ /yr progression and 8˚ /yr of kyphosis
- *Wilde et al, Spine 1994*
  - Vertebral subluxation, disc wedging and peripheral skeletal dystrophy prognostic factors that predict progression after arthrodesis

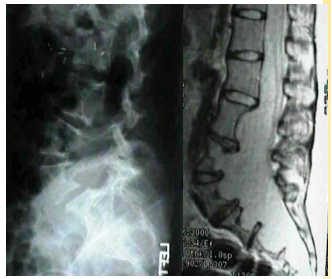


Radiographic characteristics of dystrophic scoliosis

- Certain radiographic characteristics have been reported to predict dystrophic scoliosis, but the inter-observer reliability is not well described.
- Rating systems should have good inter-rater reliability to be generalizable.
- Careful validation of these predictive factors may facilitate early detection and timely intervention to optimize outcomes and minimize delayed treatment.

Table 2. NINE RADIOGRAPHIC CHARACTERISTICS OF DYSTROPHIC DEFORMITY IN NF1.

Characteristics	% incidence
Rib penciling	62
Vertebral rotation	51
Posterior vertebral scalloping	31
Vertebral wedging	36
Spindling of transverse processes	31
Anterior vertebral scalloping	31
Widened intervertebral foramina	29
Enlarged intervertebal foramina	25
Lateral vertebral scalloping	13



From Durrani AA, Crawford AH, Choudry SN, et al. Modulation of spinal deformities in patients with Neurofibromatosis type 1. Spine 2000:25:69-75

Objective

The purpose of this study is to assess the inter-observer reliability of 8 radiographic characteristics of dystrophic modulation in NF1.

Materials and Methods

- Multicenter contribution
- 122 sets (AP & Lat) of patient radiographs with NF1 & scoliosis assessed by 5 Spine surgeons
- 8 Radiographic characteristics dystrophic scoliosis
- Blinded to final diagnosis
- Inter-observer reliability analysis was performed using Fleiss' kappa.

- **Vertebral wedging**
- **Vertebral rotation**
- **Sharp angular curve**
- **Rib penciling**
- **Vertebral scalloping**
- **Widened interpedicular distance**
- **Atypical location**
- **Spindling of transverse processes**

Inter-observer

- Of the 122 cases, 83(68%) were dystrophic and 39(32%) were non-dystrophic.
- Overall agreement for dystrophic diagnosis was 0.61(good).

Characteristic	Fleiss' kappa
Dystrophic diagnosis	0.612
Vertebral wedging	0.619 - max
Vertebral rotation	0.589
Sharp angular curve	0.602
Rib penciling	0.414
Vertebral scalloping	0.140 - min
Widened interpedicular distance	0.182
Atypical location	0.276
Spindling of transverse processes	0.424

Results

- For dystrophic diagnosis
  - all 5 readers agreed that a case was dystrophic in 46 of 122 cases, and non-dystrophic in 30 of 122 cases,
  - but there was some disagreement in 46 cases.
- For wedging, where the agreement was ‘good’, the readers completely agreed more than half of the time.
- In contrast, where the agreement was ‘poor’, the readers disagreed in nearly all the cases.

Actual Dystrophic diagnosis

Variable Name	Rate observed in all 610 readings	Rate observed in truly dystrophic (sensitivity)	Rate observed in truly non-dystrophic (1-specificity)
Vertebral wedging	61.5 %	75.9 %	30.8 %
Vertebral rotation	61.2	76.1	29.2
Sharp angular curve	52.5	65.3	25.1
Rib penciling	42.8	54.4	18.0
Vertebral scalloping	40.7	46.8	27.7
Widened interpedicular distance	36.1	43.9	19.5
Atypical location	22.3	29.6	6.7
Spindling of transverse processes	15.1	18.3	8.2

The association between each characteristic and <u>true</u> dystrophic diagnosis is highly significant (chi-square test, p-value < 0.0001) for seven of the eight characteristics, and slightly less significant (p-value = 0.0011) for the eighth (spind).

Discussion: Dystrophic Modulation

- *Durrani et al, Spine 2000*
  - Modulation occurred 65% of patients
  - Modulation occurred in 81% of patients scoliosis presented before 7 years and 25% after 7 years
  - Rib penciling only factor influenced progression
  - Progression rate: scoliosis 12˚ and kyphosis 8˚

- Dystrophic modulation may explain underestimation of dystrophic diagnosis by 5 raters.

Summary

- Overall dystrophic diagnosis can be reliably assessed by radiographic characteristics.
- Some radiographic characteristics, such as wedging, can be reliably assessed with good agreement.
- The agreement on other characteristics, such as scalloping, is poor.

Thank you

1. Akbarnia BA, Gabriel KR, Beckman E, Chalk D. Prevalence of scoliosis inNeurofibromatosis.Spine. 1992 Aug;17(8 Suppl):S244-8

2. Brooks HL, Azen SP, Gerberg E. et al. (1975): Scoliosis: a prospective epidemiological study. J Bone Joint Surg Am 57:968-972.

3. Carey JC, Viskochil DH. 1999. Neurofibromatosis Type 1: A Model Condition for theStudy of the Molecular Basis of Variable Expressivity in Human Disorders. Am J MedGenet 89:7-13

4. Cummings RJ, Loveless EA, Campbell J, Samelson S, Mazur JM. Interobserver reliability and intraobserver reproducibility of the system of King et al. for the classification of adolescent idiopathic scoliosis. J Bone Joint Surg Am. 1998 Aug;80(8):1107-11.

5. Crawford AH, Herrera-Soto J. Scoliosis associated with neurofibromatosis. Orthop Clin North Am. 2007 Oct;38(4):553-62

6. Crawford A. H. Pitfalls of spinal deformities associated with neurofibromatosis in children. Clin Orthop 1989; 245: 29-42.

7. Dang NR, Moreau MJ, Hill DL, Mahood JK, Raso J. Intra-observer reproducibility and interobserver reliability of the radiographic parameters in the Spinal Deformity Study Group's AIS Radiographic Measurement Manual. Spine. 2005 May 1;30(9):1064-9.

8. Durrani AA, Crawford AH, Choudry SN, et al. Modulation of spinal deformities in patients with neurofibromatosis type 1. Spine 2000:25:69–75

9. Friedman JM. 1999. The epidemiology of neurofibromatosis type 1. Am J Med Genet 89:1-6

10. Easton DF, Ponder MA, Huson SM, Ponder BAJ. 1993. An analysis of variation in expression of neurofibromatosis type 1(NF1): evidence for modifying genes. Am J Hum Genet 53:305–313.

11. Gstoettner M, Sekyra K, Walochnik N, Winter P, Wachter R, Bach CM. Inter- and intraobserver reliability assessment of the Cobb angle: manual versus digital measurement tools. Eur Spine J. 2007 Oct;16(10):1587-92. Epub 2007 Jun 5.

12. Gupta MC, Wijesekera S, Sossan A, Martin L, Vogel LC, Boakes JL, Lerman JA, McDonald CM, Betz RR. Reliability of radiographic parameters in neuromuscular scoliosis. Spine. 2007 Mar 15;32(6):691-5.

14. Joseph K. N., Bowen J. R., MacEwen G. D. Unusual orthopedic manifestations of neurofibromatosis. Clin Orthop 1992; 278: 17-28.

15. Kane WJ (1977): Scoliosis prevalence: a call for a statement of terms. Clin Orthop 126:43-46.

16. Kane Wj, MoeJH (1970): A scoliosis-prevalence survey in Minnesota.Clin Orthop 69,216-218.

17. Kim H. W., Weinstein S. T. The management of scoliosis in neurofibromatosis. Spine 1997; 22: 2770-2776.

18. Lenke LG, Betz RR, Bridwell KH, Clements DH, Harms J, Lowe TG, Shufflebarger HL. Intraobserver and interobserver reliability of the classification of thoracic adolescent idiopathic scoliosis. J Bone Joint Surg Am. 1998 Aug;80(8):1097-106.

19. National Institute of Health Consensus Development Conference. NF-1. 1988. p. 172–8.

20. Polly DW Jr, Kilkelly FX, McHale KA, Asplund LM, Mulligan M, Chang AS. Measurement of lumbar lordosis. Evaluation of intraobserver, interobserver, and techniique variability. Spine. 1996 Jul 1;21(13):1530-5; discussion 1535-6.