

### Are Serum Ion Levels Elevated in Pediatric Patients with Growing Spine Implants versus Controls?

<u>Smitha Mathew, MBBS</u>\*; A. Noelle Larson, MD\*; Bangke Zhang, MBBS\*; Yong Xie, MBBS\*; Matthew P. Abdel, MD\*; Andre van Wijnen, PhD\*; Todd A. Milbrandt, MD,MS\*; Geoffrey Haft ,MD† \* Mayo Clinic, Rochester, MN; † Sanford USD Medical Center, Sioux Falls, SD

Supported by: T. Denny Sanford Pediatric Collaborative Research Fund

### **Disclosures**

 I (and/ or my co-authors) have something to disclose.

 Refer to the ICEOS Annual Meeting program for more detailed disclosure information.



### Introduction

### Children with spinal fusion – elevated serum Ti levels.



Spine (Phila Pa 1976). 2013 Apr 1;38(7):564-70. doi: 10.1097/BRS.0b013e3182741961.

Serum titanium, niobium, and aluminum levels after instrumented spinal arthrodesis in children.

Cundy TP1, Antoniou G, Sutherland LM, Freeman BJ, Cundy PJ.

Eur Spine J. 2014 Nov;23(11):2393-2400.

MAY CLIN Serum titanium, niobium and aluminium levels two years following instrumented spinal fusion in children: does implant surface area predict serum metal ion levels?

Cundy TP, Cundy WJ, Antoniou G, Sutherland LM, Freeman BJ, Cundy PJ.

### Introduction

- Children with spinal fusion elevated serum Ti levels.
- Corrosion → metal debris → increased Ti ions





### Introduction

### • What about **Cobalt** and **Chromium**?





### **Hypothesis**

 Serum ion levels will be elevated in pediatric patients with spinal implants, particularly growing spine devices compared to patients with implants in the extremities.





 Intra-op waste tissue specimens: metal debris + macrophage activity

MAYO CLINIC



Tissue biopsies were obtained from the site of metal debris adjacent to the implant



### **Study Population**

### Patients were enrolled at two centers prior to surgery.



### **Study Population**

Pediatric patients undergoing surgery **N = 51** 









### **Results – Do ion levels change?**





### **Results**

### Before and after spine instrumentation (DeNovo) (N = 8)

Metal	Before implantation	After implantation	p values
Cobalt (N = 0-0.9 ng/ml)	0.3 ng/ml	1.0 ng/ml	0.06
Chromium (N < 0.3 ng/ml)	0.2 ng/ml	0.3 ng/ml	0.28
(N < 1 ng/ml)	0.91 ng/ml	3.3 ng/ml	0.02

### Results

### Growing spine implants vs Fusion + Controls

	Metal	Growing spine implants (N = 11)	Others (Fusion + Controls) (N = 30)	p values
	Cobalt (N = 0-0.9 ng/ml)	0.63 ng/ml	0.32 ng/ml	0.052
	Chromium (N < 0.3 ng/ml)	1.2 ng/ml	0.27 ng/ml	0.01
MAX CLIN T	Titanium (N < 1 ng/ml)	3.3 ng/ml	1.9 ng/ml	0.01

### Results

Growing spine implants vs Extremity Implants (Controls)

Metal	Growing spine implants (N = 12)	Extremity implants (Controls) (N = 26)	p values
Cobalt (N = 0-0.9 ng/ml)	0.63 ng/ml	0.275 ng/ml	0.023
Chromium (N < 0.3 ng/ml)	1.018 ng/ml	0.27 ng/ml	0.008
Titanium (N < 1 ng/ml)	3.1 ng/ml	1.1 ng/ml	0.007

# Histology – H&E stain (10X)Flexible Ti NailGrowing Rod







### Histology – SEM (10 uM) **Growing Rod**





### Intracellular metal particles Growing Rod







H&E (40X)

SEM 100 um

### Immunohistochemistry – CD68 (macrophage marker)





**Growing Rod** 

### Immunofluorescence – Growing Rod IgG (control) 40x



CD68 (macrophage marker) 40x





### IL-6 (inflammatory marker) 40x



### DAPI







### Conclusion

 Growing spine implants create an increase in serum levels of titanium, chromium, and cobalt ions compared to controls.

 Tissue evaluation reveals high macrophage activity and intracellular metal particles.



### **Discussion**

### Previous series

- Patients with GR and MCGR vs controls (non operated patients)
- Elevated serum Ti metal ions

Spine Deform. 2018 Jan;6(1):48-53. doi: 10.1016/j.jspd.2017.06.005.

Metal Ion Release During Growth-Friendly Instrumentation for Early-Onset Scoliosis: A Preliminary Study.

Yilgor C<sup>1</sup>, Efendiyev A<sup>2</sup>, Akbiyik F<sup>3</sup>, Demirkiran G<sup>2</sup>, Senkoylu A<sup>4</sup>, Alanay A<sup>1</sup>, Yazici M<sup>5</sup>.



### **Discussion**

### Previous series

- Patients with VEPTR and MCGR
- Elevated serum Ti metal ions (VEPTR > MCGR)
- No control group

J Pediatr Orthop. 2019 Nov 1. doi: 10.1097/BPO.00000000001463. [Epub ahead of print]

Elevated Serum Titanium Levels in Children With Early Onset Scoliosis Treated With Growthfriendly Instrumentation.

Li Y<sup>1</sup>, Graham CK, Robbins C, Caird MS, Farley FA.



### Discussion

- Reasonable to consider growing spine implant removal and converting to a fusion surgery at maturity.
  - Retaining an implant → lifetime exposure to serum metal ions → consequences??



## THANK YOU !





