VOLUME 20, ISSUE 20 | NOVEMBER 12, 2024

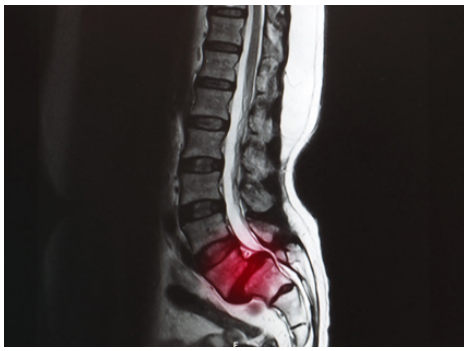
Orthopedics This Week

WEEK IN REVIEW

4 Exactech Declares Bankruptcy >> In a bid to fend off more than 2,200 pending lawsuits, Exactech's owner, TPG Capital, which acquired Exactech in 2018 for $737 million, has decided to put the Company into bankruptcy. While bankruptcy typically spells the end of a company, in this case, it, potentially, gives this venerable orthopedic pioneer a fresh start.

7 Best New Spine Technologies: Silver Medal Winners >> Here are the best spine technologies for 2024, Silver Award Winners. These represent the most promising, innovative and exciting new technologies for improving spine care for 2024.

15 Phase 3 Enrollment Done for 1st Intradiscal Back Pain Injection >> Phase 3 enrollment of 417 patients for the landmark MODEL trial of a novel peptide intradiscal injection for low back pain is now completed. Study sponsor, Spine BioPharma, Inc., made this announcement at the recently concluded 2024 North American Spine Society annual meeting.



BREAKING NEWS

For all news that is ortho, read on.

CLICK HERE TO DOWNLOAD A PDF VERSION OF THIS WEEK'S NEWSLETTER

Orthopedic Power Rankings

Robin Young's Entirely Subjective Ordering of Public Orthopedic Companies

THIS WEEK: Big price moves this past month. A handful of firms posted up stellar sales growth numbers and in the specific case of Alphatec Spine, better-than-expected Q3 cash flows. Indeed, as we noted on August 8th in an article titled: The Smartest Guys in Spine Are Buying ATEC, insiders bought 79,000 shares at around $6.30/share. Today, ATEC is $9.81 / share. That's a 77% jump in 30 days. For those insiders, my guess is that they made $270k profit. Lesson: when the insiders are buying, which is public information, odds are that company is worth more than Wall Street thinks.

RANK	LAST WEEK	COMPANY	TTM OP MARGIN	30-DAY PRICE CHANGE	COMMENT
1	2	Integra LifeSciences	6.60%	36.91%	IART, broken stock, but not broken company, up 37% on news of a new CEO Mojdeh Poul. Q3's sales and EPS report was ugly, but cash flow came in strong, 16% of sales.
2	1	Pacira Biosciences	13.02	10.65	Despite a near miss on sales, cash flow was strong and PCRX received good reimbursement news from CMS for Exparel. Also new CFO announced, Shawn Cross.
3	4	Globus Medical	18.72	14.82	GMED generated $204 million net cash from operations for Q3—and, I suspect, management wants more. Wall Street is still not giving GMED the valuation it deserves.
4	6	Orthofix	(10.99)	28.71	Up 29% in the last month, big vote of confidence in CEO Calafiore's accomplishments. Q3 sales up 7%, EBITDA hit $19 milliion and a new term loan was signed with bankers.
5	5	Medtronic	19.17	(0.71)	MDT will be announcing quarterly results in a week and most analysts are looking for sales to grow at roughly spine industry rates—possibly higher.
6	7	Zimmer Biomet	20.70	4.56	ZBH's sales rose 4.1% to $1.8 billion, essentially in line with industry rates. Z1 Femoral Hip System launched at AAHKS. OrthoGrid deal closed. Valuation remains low.
7	3	Bioventus	4.34	3.05	For Q3, sales increased 15%, 4th quarter in a row of double-digit sales growth. Cash flow was $10 million to the positive vs a $9 millon burn for the same quarter last year.
8	8	Johnson & Johnson	20.78	(3.22)	For Q3 DePuy Synthes highlights were Trauma +5.3%, Knees + 5.2% and Spine +4.5%. Lowlights were Hips +3.0%. Two product highlights: VELYS™ and Teligen™.
9	NR	Alphatec Spine	(20.35)	77.02	Sale up a very impressive 27%, $7 million in EBITDA, $81 million cash in the bank and a new term loan. Again, #1 market share gainer in Spine.
10	9	Stryker	21.19	6.22	Q3 sales growth was good, up a strong 11.9%. Operating profit margin rose. But...board member Rhonda Stryker sold nearly $261 million in stock. My guess, estate planning.

Robin Young's Orthopedic Universe

TOP PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	Alphatec Holdings	ATEC	$9.40	$1,333	77.02%
2	Aurora Spine	ASG.V	$0.31	$24	55.62%
3	Integra LifeSciences	IART	$24.78	$1,912	36.91%
4	Paragon 28	FNA	$7.15	$597	36.19%
5	Orthofix	OFIX	$19.41	$742	28.71%
6	SI-BONE, Inc	SIBN	$15.32	$639	19.31%
7	ConMed	CNMD	$73.43	$2,268	16.59%
8	Globus Medical	GMED	$80.88	$11,013	14.82%
9	Pacira Biosciences	PCRX	$17.24	$796	10.65%
10	Aclarion	ACON	$0.19	$2	8.25%

WORST PERFORMERS LAST 30 DAYS

	COMPANY	SYMBOL	PRICE	MKT CAP	30-DAY CHG
1	Anika Therapeutics	ANIK	$17.26	$253	-32.39%
2	Smith & Nephew	SNN	$24.29	$10,619	-15.89%
3	Xtant Medical Hldgs	XTNT	$0.53	$73	-12.45%
4	Medacta	MOVE	$127.82	$2,556	-10.92%
5	MicroPort Scientific	853	$0.86	$1,582	-9.19%
6	AxoGen	AXGN	$12.66	$557	-7.79%
7	Johnson & Johnson	JNJ	$155.47	$374,313	-3.22%
8	Medtronic	MDT	$87.72	$112,498	-0.71%
9	Bioventus	BVS	$11.82	$959	3.05%
10	SINTX Technologies	SINT	$2.89	$4	4.33%

LOWEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Pacira Biosciences	PCRX	$17.24	$796	12.52
2	Johnson & Johnson	JNJ	$155.47	$374,313	20.29
3	Medtronic	MDT	$87.72	$112,498	21.12
4	ConMed	CNMD	$73.43	$2,268	24.87
5	Zimmer Biomet	ZBH	$108.18	$21,536	26.21

HIGHEST PRICE / EARNINGS RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	P/E
1	Xtant Medical Hldgs	XTNT	$0.53	$73	110.44
2	Globus Medical	GMED	$80.88	$11,013	55.35
3	Medacta	MOVE	$127.82	$2,556	41.90
4	Smith & Nephew	SNN	$24.29	$10,619	40.38
5	Stryker	SYK	$375.96	$143,322	36.38

LOWEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Integra LifeSciences	IART	$24.78	$1,912	-7.84
2	Pacira Biosciences	PCRX	$17.24	$796	1.16
3	ConMed	CNMD	$73.43	$2,268	1.30
4	Medacta	MOVE	$127.82	$2,556	1.50
5	Stryker	SYK	$375.96	$143,322	3.14

HIGHEST P/E TO GROWTH RATIO (EARNINGS ESTIMATES)

	COMPANY	SYMBOL	PRICE	MKT CAP	PEG
1	Johnson & Johnson	JNJ	$155.47	$374,313	6.76
2	Xtant Medical Hldgs	XTNT	$0.53	$73	5.52
3	Medtronic	MDT	$87.72	$112,498	3.83
4	Zimmer Biomet	ZBH	$108.18	$21,536	3.82
5	Smith & Nephew	SNN	$24.29	$10,619	3.57

LOWEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	Dynatronics Corp	DYNT	$0.13	$1	0.03
2	Nevro Corp	NVRO	$5.08	$189	0.45
3	Xtant Medical Hldgs	XTNT	$0.53	$73	0.80
4	Orthofix	OFIX	$19.41	$742	0.99
5	Pacira Biosciences	PCRX	$17.24	$796	1.18

HIGHEST PRICE TO SALES RATIO (TTM)

	COMPANY	SYMBOL	PRICE	MKT CAP	PSR
1	Aclarion	ACON	$0.19	$2	25.42
2	Globus Medical	GMED	$80.88	$11,013	7.02
3	Stryker	SYK	$375.96	$143,322	6.99
4	Medacta	MOVE	$127.82	$2,556	5.01
5	SI-BONE, Inc	SIBN	$15.32	$639	4.60

PSR: Aggregate current market capitalization divided by aggregate sales and the calculation excluded the companies for which sales figures are not available.

Exactech Declares Bankruptcy

BY ROBIN YOUNG

In a bid to fend off more than 2,200 pending lawsuits, Exactech, Inc.'s owner, TPG Capital, which acquired Exactech in 2018 for $737 million, has decided to put the company into bankruptcy.

While bankruptcy typically spells the end of a company, in this case, it, potentially, gives this venerable orthopedic pioneer a fresh start.

Exactech's Fight for Survival

Arrayed against Exactech are more than 2,200 pending lawsuits which allege defective implants and injured patients. Approximately 80% of these lawsuits (1,770) are aggregated as a multi-district litigation (MDL) in the U.S. District Court for the Eastern District of New York. The remaining cases are in Florida (595), Illinois (24), and other states (28).

None of these cases have yet been adjudicated. No court has ruled that these claims are true.

Exactech denies the allegations.

The federal courts consolidated the lawsuits into an MDL to reduce costs and streamline the legal process. The MDL includes individual lawsuits, but unlike a class action, the lawsuits can proceed separately.

District Judge Nicholas G. Garaufis, who is overseeing the MDL, has selected four cases for bellwether trials, which are scheduled to begin in 2025.

Exactech's Product Recall and FDA Warnings

On March 23, 2023, the U.S. Food and Drug Administration (FDA) issued a reminder to surgeons and patients that Exactech's joint replacement implants manufactured by Exactech between 2004 and August 2021 and recalled in 2021 and 2022 were defective.

Courtesy of Exactech, Inc.

According to the FDA, many of Exactech joint replacement devices (including knees, ankles, and hips) were packaged in defective packaging bags. The defective bags were missing one of the oxygen barrier layers that protect devices from oxidation, which is a chemical reaction with oxygen that can degrade plastics over time.

Oxidation can lead to accelerated device wear/failure, and component cracking or fracture, all leading to corrective revision surgery.

The FDA reminded surgeons and patients that Exactech's recalled devices were associated with increased risk of revision surgeries and bone loss related to excessive device wear/failure.

Exactech began its recall of potentially defective devices in 2021, specifically:

- In June 2021, Exactech recalled some GXL Liners for Novation, Acumatch, and MCS hip replacement devices due to excessive and premature wear but the root cause was unknown.
- On February 7, 2022, Exactech expanded the voluntary recall to all Optetrak, Logic, and Truliant knee replacements and Vantage total ankle replacements packaged in defective bags regardless of a device's label or shelf life. Exactech recalled the devices because around 80% of the knee

and ankle replacement devices manufactured since 2004 were packaged in defective bags. Devices packaged in defective bags can lead to oxidation over time that results in the potential risks listed above.

- In August 2022, Exactech expanded the hip replacement device recall to include all hip devices with polyethylene components packaged in defective bags.

The FDA then issued the following recommendations to surgeons and patients:

- Do not implant any knee, ankle, and hip devices recalled by Exactech.
- Do not remove well-functioning Exactech joint replacement devices from patients who do not have any new or worsening pain or symptoms.
- Monitor patients who have any implanted devices manufactured by Exactech between 2004 and August 2021 for potential device wear, failure, or bone loss. Consider performing X-rays to further evaluate a patient and their implanted device if you suspect a failed device.
- Discuss revision surgery with patients who may have worsening pain or joint weakness that is potentially attributable to the device based on clinical exam, on a case-by-case basis. As a part of shared decision-making, discuss the benefits and risks of all relevant treatment options with your patients.
- Remove all recalled devices from inventory and return to Exactech.

How Bankruptcy Will Save Exactech

Exactech, which was founded in 1985, has been one of the most admired and respected orthopedic implant companies in the world. Founded by Bill Petty, M.D., Gary Miller, Ph.D. and Betty Petty, the company developed a reputation as a trusted "surgeon's company." In many ways, the company epitomized old fashioned values of integrity, accountability and innovation to serve patients and the surgeons who care for them.

It was a culture that came directly from its founders.

Dr. Petty, specifically, made his early reputation in academic research. Through Exactech and his activities in such organizations as the Orthopedic

Research and Education Foundation, he has been a steady champion for improving orthopedics in all its manifestations.

Chapter 11 bankruptcy will allow Exactech to operate as normal, serving orthopedic surgeons and their patients. It relieves Exactech from non-operating legacy liabilities, has brought in new capital ($85 million from an investor group) and will make sure that the plaintiff's bar doesn't get between Exactech and its surgeon customers.

According to Exactech's President and CEO Darin Johnson, "Despite the strength of the underlying business, we face unsustainable liabilities associated with knee and hip litigation related to the packaging recalls we voluntarily initiated between 2021 and 2022. We take our commitment to patient well-being very seriously and have provided substantial out-of-pocket patient reimbursements and surgeon support for related expenses."

The bankruptcy process, said Johnson, "Is intended to help us create a stronger foundation for long-term growth with an improved balance sheet and new capital as well as ensure that we can continue providing innovative, industry-leading implants for surgeons and their patients for years to come."

Final Observation

One of the goals of the plaintiff's bar in these types of litigation is to overwhelm the target company and force it into settlement talks—and to do so, if possible, BEFORE the cases are tried in court. In past cases of mass tort litigation—the breast implant cases or the pedicle screw litigation cases—the plaintiff's allegations ultimately proved to be either wrong or vastly overstated.

Exactech lives to fight another day. Which is essential for all of orthopedics.

For more information about past mass tort litigation efforts see *OTW*'s "Biggest Lawsuit in Spine History: The Pedicle Screw Litigation Part I" and "Biggest Lawsuit in Spine History: Pedicle Screw Litigation Part II." ♦

Best New Spine Technologies: Silver Medal Winners

BY ROBIN YOUNG

OTW's 2024 Best Spine Technology Silver Award winners represent some of the most innovative, practical and significant products in spine care. / Source: Pixabay

Here are the best new spine surgery technologies for 2024, Silver Medal Winners.

Every year *Orthopedics This Week* convenes a panel of top surgeons to review dozens of new technology submissions from around the world.

This award was inaugurated more than a decade ago to recognize the inventors, engineering teams, surgeons and their companies who have created the most innovative, enduring, and practical products to treat back care.

To win the *Orthopedics This Week* Best New Technology Award for spine care, a new technology must score highly for each of the following criteria:

1. Be creative and innovative.
2. Bring long term significance to treating spine pathologies. Does this technology have staying power?
3. Solve a current clinical problem.
4. Improve standard of care
5. Be cost effective?
6. Members of the judges panel would consider personally using it.

We received a record number of submissions for 2024.

Our judges this year were:

The Judges

Peter Derman, M.D.: A minimally invasive and endoscopic spine surgeon at Texas Back Institute, an honors graduate from Stanford University, a graduate of the Perelman School of Medicine at the University of Pennsylvania and concurrently an MBA grad from the Wharton School of Business, Dr. Derman is a key surgeon opinion leader and dedicated physician-researcher, exploring

(L to R): Peter Derman, M.D., Stephen Hochschuler, M.D., Isaac Moss, M.D., Kris Radcliff, M.D., Juan Uribe, M.D., and Michael Wang, M.D., M.B.A.

ways to better medicine for future generations.

Stephen Hochschuler, M.D.: Co-founder and chairman of the board of the Texas Back Institute, Stephen Hochschuler, M.D., is a graduate of Columbia College in New York, a Harvard Medical School graduate and pioneer in modern spine surgery. He began his private practice since 1977 and taught at the University of Texas Health and Science Center Southwestern Medical School. He founded and mentored dozens of medical companies.

Isaac Moss, M.D.: Dr. Moss is Chair, Department of Orthopaedic Surgery, Professor of Orthopaedic Surgery, Co-Director of University of Connecticut's Comprehensive Spine Center. Dr. Moss is a fellowship trained spine surgeon at the UConn Musculoskeletal Institute. Dr. Moss graduated from University of Toronto, was the department's top graduate, then trained at Rush University Medical Center in Chicago. Dr. Moss's master's degree is in biomedical engineering. He has received many awards and scholarships for his contributions to cutting edge research for novel biologic therapies for intervertebral disc degeneration.

Kris Radcliff, M.D.: Dr. Kris Radcliff is an internationally recogized spine surgery thought leader, full professor in the Department of Neurological Surgery at Thomas Jefferson University, an honors graduate from Harvard College, a graduate of Duke University's School of Medicie on a prestigious Dean's Tuition Scholarship, a Baylor College of Medicine resident and, before founding the Spinal DISC center, Dr. Radcliff was a spine surgery fellow at the Rothman Orthopaedic Institute.

Juan Uribe, M.D.: Juan Uribe, M.D., is Chief of the Division of Spinal Disorders, Volker K. H. Sonntag Chair for Spine Research, and Vice Chairman of Neurosurgery at Barrow Neurological Institute. He was named President and Chair of the AANS/CNS Section on Disorders of Spine and the Peripheral Nerves in 2024. Dr. Uribe earned his medical degree from Kris Ra in Colombia, completed residency at Hospital San Vicente de Paul and, later, at the University of South Florida and a fellowship at the University of Miami.

Michael Wang, M.D., M.B.A.: Michael Y. Wang, M.D., FACS is Chief of Neurosurgery, University of Miami Hospital Spine Neurosurgery Fellowship Director and Professor with Tenure, Departments of Neurosurgery and Rehab Medicine. Dr. Wang earned both his BS and MD degrees from Stanford University, residency at the University of Southern California, fellowship at the University of Miami. He has held many leadership roles at multiple surgeon societies and has edited 12 medical textbooks, authored over 600 publications in the medical literature.

Best New Spine Surgery Technologies:
SILVER MEDAL WINNERS

NuvoDisc Microgel

Inventors: Wesley Sierk, Eric Olson, Jeff Zisselman, and Nick Manesis / **Engineers:** Nick Manesis / **Clinician Developers:** John Edwards, M.D. Mark Stouffer, M.D. Jon Obray, M.D., Rick Obray, M.D. Derek Freiden, M.D.

How it Improves Spine Surgery: NuvoDisc is an entirely novel outpatient approach to creating and maintaining disc height thereby providing stability and support for patients with degenerative disc disease.

The NuvoDisc Microgel is comprised of microspheres of polymethylmethacrylate (PMMA) with Pluronic F127 hydrogel. The refrigerated compound flows into the disc space through a 7" spinal needle and then cures to a flexible semi-solid at body temperature.

Using NuvoDisc, DDD patients can be treated in an ambulatory surgical center or pain clinic. No large incisions, painful surgical recovery or physical therapy which are often required for more traditional spine surgery treatments for lower back pain.

Company: 33 Medical Inc.

Website: www.33medicalinc.com

NuvoDisc Microgel

SPIRA-A Integrated Fixation System

Inventors: Seth Anderson, Anthony Solt, Brooks McAdam, Kurt Faulhaber, and Steven Willis / **Engineers:** Anthony Solt

How it Improves Spine Surgery: The SPIRA-A Integrated Fixation system uses a novel arch-based structure and a highly differentiated surface topography and science to encourage bone cell proliferation AND uniform load distribution across endplates. SPIRA-A Integrated is designed for the ALIF approach.

Its integrated fixation supports a traditional ALIF approach. Its windswept cage geometry facilitates accessing L5-S1 with difficult vascular anatomy. SPIRA-A is part of a comprehensive solution to anterior column reconstruction. It's a complete system of cages, fixation and instrumentation. Implants at multiple heights, footprints, shapes and lordotic angles to accommodate different patient anatomy.

Company: Camber Spine

Website: www.cambermedtech.com

Mindy Elgart, Chad Spear, Drue DeAngelis, Brooks McAdam, Jacob Forstat, and Robin Young

Canturio® Lumbar Cartridge

Inventors: Jeffrey M. Gross, Peter J. Schiller, Mark A. Adler and Kevin Gemmell / **Engineers:** Jeffrey M. Gross, Peter J. Schiller, Mark A. Adler and Kevin Gemmell

How it Improves Spine Surgery: Canary Medical's Canturio Lumbar Cartridge (canturio®lc) actively senses patient movements and communicates remotely to the patient's care team—effectively delivering data regarding a patient's recovery from spinal fusion surgery between office visits.

canturio®lc is intended for use with a Lumbar Interbody System for lumbar spinal fusion from L1-S1. The cartridge collects the patient's kinematic data from the implanted medical device and communicates that data to the care team during a patient's post-surgical recovery from degenerative disc disease surgery. The data tracks fusion progression, detecting clinically relevant instability, partial fusion or non-fusion. The cartridge collects data for at least 10 years. With Canary's platform, clinicians can rank each patient's performance versus their peers based on age, gender and time since surgery.

Company: Canary Medical

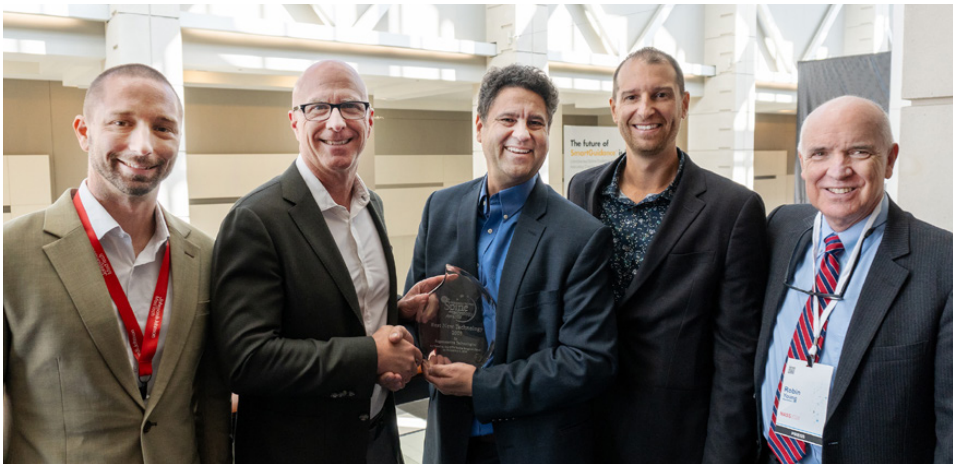
Website: www.canarymedical.com

Bill Hunter, founder of Canary Medical demonstrating canturio®lc

Teligen

Inventors: The many Teligen and Fox inventors, commercial team, and design surgeons who helped develop the system. / **Engineers:** All the engineers, past & present, who were a critical part to the technical success of Teligen.

How it Improves Spine Surgery: The Teligen System for spinal surgery provides minimally invasive access, advanced visualization, illumination, magnification, discectomy, navigation and peripheral motor nerve stimulation. This solution is centered around the disposable hands-free single use VueLIF™ camera, which allows surgeons to view and access more of the targeted anatomy through a smaller access port due to its large field of view and variable camera placement within the access port.



Shane Fleshman, Drue DeAngelis, Eric Buehlmann, John DiVincenzo and Robin Young

A larger camera field of view allows surgeons to reduce access port size, minimizing muscle/tissue disruption. TELIGEN™ also delivers improved ergonomics. Surgeons can stand naturally while viewing the 4k video monitor at eye level. The system uses a disposable camera and disposable and reusable instrument set (navigated and MMG neuromonitoring capable), capital equipment, 4k monitor, and a camera control system. A true procedural solution.

Better visualization, user centric control and streamlined instrument set. Teligen simplifies the MIS TLIF procedure so that surgeons and OR staff can deliver better patient care, more efficiently.

Company: DePuy Synthes Spine

Website: www.jnjmedtech.com/en-US/companies/depuy-synthes

EUROPA® Advanced Deformity System

Inventors: Mahesh Krishnan, Jay Yadav
Engineers: Nikolay Laubert, Wayne Gray

Randy Cochran, Robin Young, Mahesh Krishnan, Andrew Gallagher

How it Improves Spine Surgery: In complex spine surgery, rod failures and fractures lead to pain and revision surgery. In comes MiRus' EUROPA® Advanced Deformity System. Touted as the "most advanced and versatile" deformity screw system, MiRus says the system eliminates the need for quad rod constructs in deformity cases and potentially solves the PJK/PJF at the top of deformity constructs. The system is comprised of short polyaxial pedicle screws tulips manufactured from titanium, and 5.5-5.0 mm to 4.5-4.0 mm transition rod components manufactured from its proprietary metal alloy—Molybdenum-47.5Rhenium (MoRe®). Compared to titanium and cobalt chromium, MoRe® is stronger, more resistant to fatigue and has more ion release resistance, company officials said. "Better materials with optimized biomechanical, wear and biological properties result in the development of superior spinal implants and better outcomes for patients," company officials said.

Company: MiRus, LLC

Website: www.mirusmed.com

Momentum Spine

Inventors: Evan Dimentberg, Dr. Jean Ouellet and Philippe Miller, Frank de Wijk and Leander Goor

How it Improves Spine Surgery: Using an artificial intelligence-based digital health application, this app connects scoliosis patients to their physician remotely. It employs a smartphone camera to recreate a true-to-scale 3D model of the torso from a video and then the app's proprietary algorithms analyze 3D topography to predict the internal anatomy of the spine.

Symon Stowe, Sabina Fehric, Dr. Jean Ouellet, Caitlyn Stowe, Nedim Hodzic, Dr. Evan Dimentberg, Frank de Wijk, Philippe Miller, Sylvain LeBeux, Oliver Levy

In other words, Momentum Spine quantifies the extra-spinal deformities (what we can see from the outside) and correlates them to the Cobb Angle (what we can only see on X-rays) to predict the progression of the scoliotic deformity. No radiation, at-home scans allow spine care teams to rapidly detect changes in spinal curvatures and implement conservative treatments. Furthermore, Momentum Spine's imagery-guided AI predictions can determine severity and improve intervention timing, and both optimize and personalize care.

Company: Momentum Health

Website: momentum.health/about

MSKai

Inventors: Chip Wade, Ph.D.; John Burrow, D.M., Adam Bruggeman, M.D., Sreenivas Rangan Sukumar, and Larry Roberts / **Engineers:** Larry Roberts, Sreenivas Rangan Sukumar, Glenn Osga, and Adrien Guerard

How it Improves Spine Surgery: MSKai makes the care pathway for treating musculoskeletal pathologies more efficient. Currently focused on the spine, MSKai improves identification, segmentation, measurement and reporting on suspected spine pathologies and abnormalities. The system uses imaging from a user portal or PACS. It then automatically labels the imaging series by anatomy, segmented into specific anatomy classifications and includes all pertinent medically relevant measurements.

Drue DeAngelis, Dr. Chip Wade, Dr. Paul Slosar, Robin Young

Once the segmentation and measurement evaluations are complete (2 to 4 seconds) a summary radiology read report, and a detailed imaging report are generated in real time. The end result is better diagnostic and treatment decisions as well as support for insurance pre-authorization and to create workflow efficiencies and increase accuracy for the radiologist.

Company: MSKai

Website: www.mskai.ai

NEXlif™

Inventors: Maahir Haque / **Engineers:** Leighton Lapierre and Brandon Arthurs

How it Improves Spine Surgery: NEXlif™ system allows surgeons to perform prone lateral spine surgery without expensive and cumbersome contralateral bolsters to control or prevent patient and spinal column motion intraoperatively. The device addresses a technical challenge and barrier to adoption of prone lateral surgery—lateral retractor migration causing psoas muscle creep or even vascular/peritoneal injury. By utilizing a patented internal fixation system, NEXlifT™ obviates the need for expensive articulating bolster systems.

NEXlif™ provides retractor stability by mechanically pairing a lateral spine retractor with a pedicle based posterior distractor. The system interfaces with a pedicle-based distractor, which allows for techniques not currently possible, including compression and distraction across the disc space. The distractor prevents the disc space from reverting/collapsing after discectomy instrument and/or trial removal. It gives the surgeon an accessible approach to either side of the anterior column for last minute changes.

Maahir Haque, M.D. and Robin Young

Company: NEXlif LLC

Website: www.nexlif.com

Piezoelectric Spinal Interbody

Inventors: Ziev Moses, M.D. and Lance Smith, M.D. / **Engineers:** Kevin Chappuis and Lucas Diehl

How it Improves Spine Surgery: With the potential for faster healing and more robust fusions using electrical signaling directly from the implant, Spark Spine is pursuing the first FDA cleared piezoelectric spinal interbody that converts human body weight into surface energy.

Spark Spine uses electromechanical polymer (EMP), a biocompatible piezoelectric material, to generate electrical energy which is transferred from the implant surface to the surrounding bone. Importantly, there is no change in the form or function of the device.

Luke Diehl, Drue DeAngelis, Kevin Chappuis, Ziev Moses, M.D. and Robin Young

These electrical signals produce biomimetic cellular stimuli to recreate the natural intercellular communication with the goal of supporting osseointegration and proliferation of osteoblasts, which may lead to a faster healing process. By harnessing the body's natural forces, Spark Spine aims to support more successful patient outcomes

Company: Spark Spine LLC

Website: www.sparkspine.com

BioBraille NanoSurface Technology

Inventors: Timothy Ganey and James Robinson

How it Improves Spine Surgery: BioBraille™ Technology developed by Spectrum Spine enhances bone differentiation at the implant level by guiding cell response favoring an osteoblast phenotype while at the same time reducing fibrous proliferation at the tissue/implant interface. The result improves spinal construct stability.

BioBraille™ was designed through a femtosecond laser engraving technology. Unlike traditional surface modification methods such as blasting, chemical etching, anodization, or laser peeling, controlled surface characteristics including feature size, depth, density, roughness, and microarchitecture can be prescriptively engineered at predetermined wavelengths most appropriate for the materials being prepared.

Spectrum Spine's ablative techniques endow titanium surfaces with modifications that not only modulate but magnify biologic responses. This foundation platform assures that changes in biologic reaction remain dependent on physical surface modifications and do not result from elemental changes in the titanium alloy composition. By achieving surface contact activation as the functional asset, the use of biologics may be reduced. Moreover, the perception and concern of hypertrophic ossification away from the site of treatment is lessened.

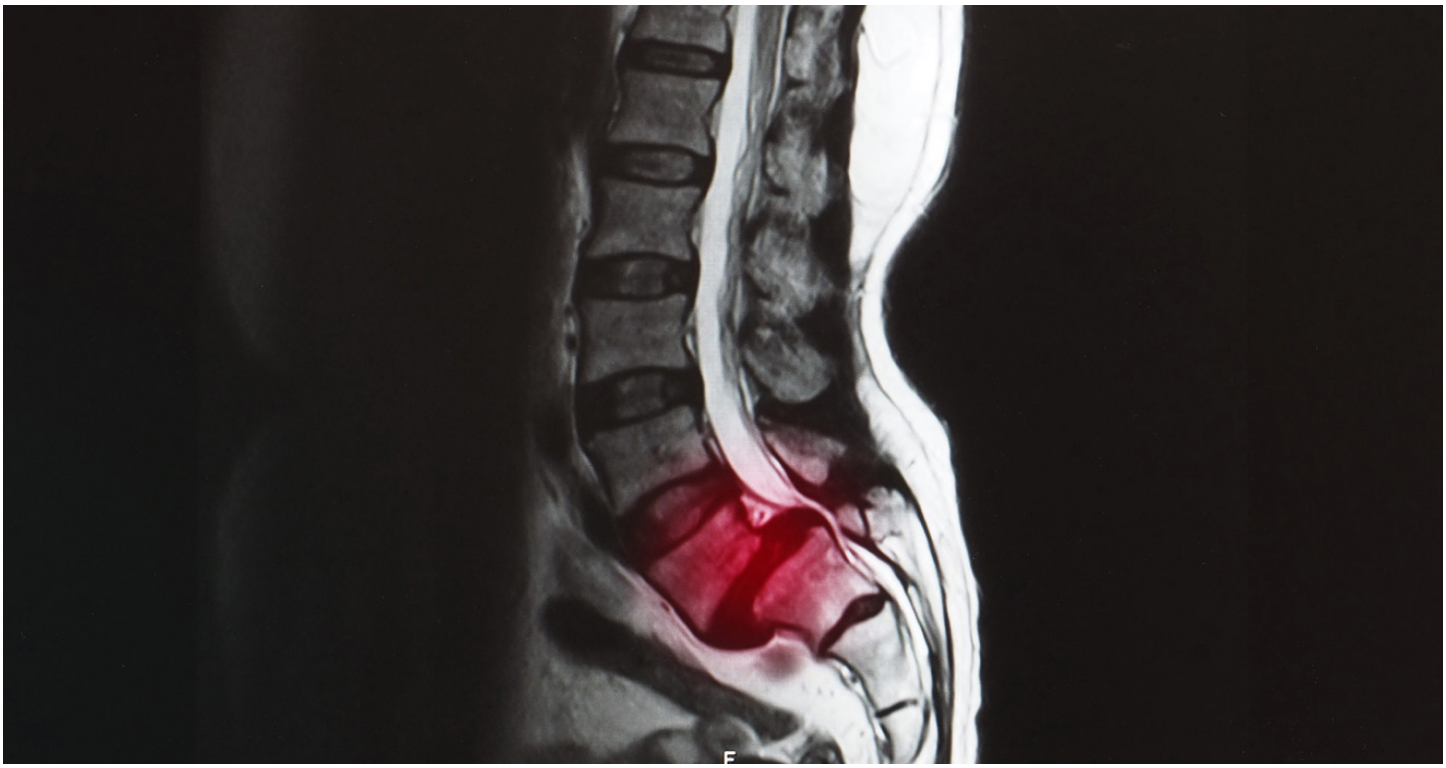
Company: Spectrum Spine

Website: www.spectrumspine.com ♦

Robin Young, Jim Robinson, and Phil Powell

Phase 3 Enrollment Done for 1st Intradiscal Back Pain Injection

BY ELIZABETH HOFHEINZ, M.P.H., M.ED.



Source: Shutterstock

Phase 3 enrollment of 417 patients for the landmark MODEL trial of a novel peptide intradiscal injection for low back pain is now completed.

Study sponsor, Spine BioPharma, Inc., made this announcement at the recently concluded 2024 North American Spine Society annual meeting.

The subject of this milestone study is a proprietary, synthetic small peptide technology named SB-01. SB-01 selectively binds and antagonizes TGF-β to reverse the negative TGF-β downstream effects in order to reduce inflammation and neuromodulate pain.

SB-01's mechanism of action may have application for such other disease states as osteoarthritis, fibrotic diseases, and oncological diseases. In animal studies, the SB-01 peptide even showed promise for regenerating the diseased disc.

Patients in the study presented with moderate-to-severe degenerative disc disease with significant pain and functional impairment. Patients were treated with a single, minimally invasive injection of the SB-01 peptide.

If the study meets its primary endpoint (at least six months low back pain relief and strong pre-clinical and clinical safety) SB-01 would be a first-to-market and best-in-class option for addressing low back pain from degenerative disc disease.

"This is an important milestone for the patient and physician community, and for the company," said Marc Viscogliosi, CEO of Spine BioPharma. "After years of conservative treatment, degenerative disc disease patients have no alternative but to ultimately undergo surgery at a high dollar cost, with long recovery periods and unpredictable outcomes."

"We are extremely pleased to have completed enrollment of the SB-01

MODEL trial ahead of schedule. This accomplishment brings SB-01 one step closer to addressing the unmet need of millions of patients who suffer from chronic low back pain associated with degenerative disc disease," he added.

The randomized, double-blind, placebo-controlled Phase 3 MODEL trial (**MO**derate – Severe Degenerative Disc **D**isease **E**valuation of the **L**umbar Spine) enrolled 417 patients at 30 U.S. investigational sites over a two-year period. SB-01 is the first intradiscal pharmacologic treatment to enter Phase 3 studies for the treatment of chronic low back pain and its associated pain-related loss of function caused by degenerative disc disease.

"Many past and current treatments for chronic low back pain do not specifically treat a major underlying cause, degenerative disc disease. There are no currently approved options that specifically target the disc itself. That's where SB-01 For Injection has the potential to be a first-in-class treatment for degenerative disc disease aimed to address associated chronic low back pain head-on," said Viscogliosi.

"With over 400 million people around the world struggling with chronic low back pain due to degenerative disc disease, there is a growing physician, patient, and industry interest in developing innovative therapies that can truly make a difference in patients' lives."

"We enrolled patients suffering from moderate- to-severe degenerative disc disease who were experiencing very significant pain and impairment in their functional activities. It is worth mentioning that this is the same type of patients we looked at in our Phase 2 study, so we are building on that foundation."

"We have several primary and secondary endpoints that consider pain intensity and pain-related function," Viscogliosi told *OTW*. "We are also collecting additional patient-reported outcomes and imaging data for subsequent analyses. The MODEL study enrolled 417 patients across 30 investigational sites in the U.S. over the past two years. Based on our assessment, other companies' clinical trial programs have taken longer to enroll a similar size population." ♦

COMPANY

New Fund Gives Voice to Innovative Physicians

A new medical technology fund which focusses on early-stage health technologies is itself an innovation. Utilizing its extensive physician network, the new fund gives voice to innovative physicians and other leaders to drive innovation in life sciences.

Meet Paul Slosar, M.D., MHCDS

OTW was able to meet with Paul Slosar, M.D., MHCDS to learn more about the fund and its vision for the future. Dr. Slosar is an orthopedic spine surgeon who practiced for 28 years in the San Francisco Bay area. He is currently a partner at FortySix Venture Capital, a multi-fund manager investing in early-stage technologies. FortySix Venture Capital manages the recently launched PhyCap. Dr. Slosar is the co-founder and a general partner of PhyCap.

Physicians Capital Fund I, LP Team Members / Courtesy of Physicians Capital Fund I LP

Beyond the operating room, Dr. Slosar has advised and positioned companies for acquisition. He spent 11 years with Titan Spine LLC as its chief medical officer. During that time the com-

pany was acquired by Medtronic. After the acquisition, he continued to work with Medtronic as a consultant and scientific strategic advisor. Dr. Slosar has provided guidance to other teams during acquisitions including Kyphon (acquired by Medtronic in 2007), Surgical Care Affiliates (acquired by UnitedHealth Group's Optum in 2017), and Relievant (acquired by Boston Scientific in 2023).

Dr. Slosar's experience as a surgeon and working business acumen has given him unique insight into the challenges and opportunities available in the healthcare industry.

How Did PhyCap Come About?

When *OTW* spoke with Dr. Slosar about the creation of PhyCap he made it clear that while he is a co-founder, the credit for the idea actually goes to its other co-founder, Dutch Rojas.

When *OTW* asked if PhyCap was Rojas' idea, Dr. Slosar told *OTW*, "Yeah, the idea was conceived by Dutch [Rojas]. We actually met at the North American Spine Society meeting in 2023 and got along instantly. We were at the same panel discussion talking about physician innovators, alternative revenue opportunities for physicians, and entrepreneurship. So it was this group of interested people all looking at innovation in healthcare, but specifically aimed at physician autonomy to be quite honest."

Rojas and Dr. Slosar immediately connected at the event and over several subsequent meetings vetted out the idea. When *OTW* asked Rojas about his inspiration for PhyCap, Rojas said, "I created the PhyCap Fund based on nearly 25 years in healthcare. As a healthcare entrepreneur with three successful exits and five founded companies, I've focused on making healthcare more affordable and accessible for everyone, everywhere."

Rojas continued, "Throughout my career, I noticed many physicians expressing frustration about not benefiting from the healthcare startup ecosystem's upside despite being crucial to its success. This realization, my commitment to physician autonomy, removal of anti-physician laws, and streamlining healthcare processes led me to create the PhyCap Fund."

Introducing PhyCap

The creation of PhyCap came less than a year after Rojas and Dr. Slosar had their

first meeting. According to Dr. Slosar, PhyCap is "structured as a traditional 10-year horizon venture capital [VC] fund." It is PhyCap's physician investor network combined with its focus on practical solutions to healthcare delivery, that makes it stand out in the VC sector.

Rojas informed *OTW,* "I formed the fund in collaboration with physicians, aiming to address two key objectives:

1. Provide physicians with opportunities to invest in and benefit from healthcare startups.

2. Deploy capital to companies that support private practices and remove barriers in the physician-patient relationship.

I saw an additional advantage in this approach: physicians involved in the fund would likely use the products of the companies we invest in, potentially contributing to their success and profitability."

"The fund is anchored by physicians," Dr. Slosar explained to *OTW,* "What I mean by that is that the majority of the people who we want to be the limited partners are physicians, or at least healthcare providers. However, this is by no means exclusive because we know the healthcare delivery chain is very complicated and includes many more pieces than physicians."

The PhyCap Team

Rojas and Dr. Slosar are executing their vision of a fund anchored by and in partnership with physicians. Dr. Slosar and four other PhyCap team members are physicians.

In addition to their medical expertise, the PhyCap physician partners also have extensive leadership and business experience. Dr. Slosar explained to *OTW*, "We have persons represented there that are men, women, various healthcare disciplines from women's health, physician owned hospitals, orthopedics, spine surgery, and another one who's come on who also has venture capital and management experience, but also is an emergency physician."

Robin Noble, M.D., MHCDS is a PhyCap team member and has been a practicing gynecologist at InterMed for more than 20 years. Dr. Noble is dual boarded in Ob/Gyn and lifestyle medicine. She completed her medical training at Columbia and Ob/Gyn residency at Yale. Dr. Noble is currently the medical director at InterMed Ambulatory Surgery Center and the chief medical advisor at Let's Talk Menopause.

Frederic Liss, M.D. is an orthopedic surgeon with 30 years of experience and a PhyCap team member. Since 2015 he has been a Castle Connolly Top Doctor®. Dr. Liss founded and led a physician-owned hospital from 2008 to 2023. He is currently the chairman of the board of directors of Physician-Led Healthcare for America (PHA).

Vipul Kella M.D., MBA is the newest PhyCap team member. Dr. Kella is a healthcare leader and emergency room physician. He is the chief medical officer of Physio AI and works with healthcare-focused industries, health tech companies, and hospitals.

By utilizing a deeply experienced physician-backed team, Dr. Slosar believes that the disconnect in healthcare innovation can be remedied. Dr. Slosar told *OTW*, "At the end of the day here, we're trying to restore agency to physicians in the process of healthcare innovation."

Dr. Slosar continued, "We [physicians] have been left out of a lot of it. Many healthcare companies are developed by tech companies and engineers, and then they bring in physicians later. PhyCap Fund aims to drive physician input and investment earlier in the process, which will result in better healthcare solutions."

Physician Led Innovation

Looking forward, Rojas has a clear vision for PhyCap. When asked about his vision for the fund, Rojas told *OTW,* "I envision PhyCap Fund achieving two main goals:

1. Physician Empowerment in Venture Capital: I aim to help physicians gain exposure and experience in venture capital. By participating in the PhyCap Fund, physicians can learn about the investment process, understand the startup ecosystem, and potentially benefit financially from successful healthcare innovations.

2. Inspiring a Physician-Led VC Movement: I envision our endeavors and results will encourage many physicians to start their venture funds. This proliferation of physician-led funds could significantly reshape the healthcare technology landscape."

Rojas added, "The underlying philosophy driving this vision is that physicians deliver healthcare technology best when they lead it. By putting physicians at the forefront of healthcare innovation and investment, we can ensure that new technologies and solutions align with the needs of healthcare providers and patients.

Through PhyCap Fund, we're not just investing in companies; we're investing in a future where physicians play a central role in shaping the direction of healthcare innovation and delivery."

PhyCap is still in its early stages. While the vision for the fund is clear, it will still be a while before the fund begins investing.

Dr. Slosar told *OTW*, "We are in active fundraising mode right now. So the fund is not investing. We are currently raising the capital in anticipation of approximately a $10 million fund close. That's our goal. We are seeing tremendous interest and commitments from investors already. Based on our current pace, we anticipate having sufficient funds to initiate investments in early 2025."

How will the funds be used? According to Dr. Slosar, "It is anticipated that the fund will be more heavily focused on the healthcare delivery side of this first. We will be investing in seed and Series A rounds. The start-ups pitching to us are very interested in our model, especially the access to an investor network of physicians and other healthcare experts. Our strategic input could be the difference between success and failure for a fledgling healthcare company."

Good Medicine Is Good Business

PhyCap was created in response to a perceived disconnect in healthcare innovation. Its founders believe that the solution to the disconnect is to give physicians a voice in healthcare innovation. That voice is what PhyCap is counting on to drive innovation. Ultimately it comes down to a simple concept and that, according to Dr. Slosar, is that "good medicine is good business." — *KD*

Miach Orthopaedics: 4,000 Patients and Counting

Westborough, Massachusetts-based Miach Orthopaedics, Inc. made news at the Orthopaedic Summit Evolving Techniques Conference 2024 by announcing that the company's Bridge-Enhanced Anterior Cruciate Ligament Restoration (BEAR) Implant not only surpassed a 4,000th patient milestone, but also achieved key end points in a recently released clinical trial.

According to Miach Orthopaedics, "The BEAR Implant is the first disruptive technology in ACL [anterior cruciate ligament] tear treatment in more than 30 years. The implant enables a torn ACL to heal and restores the natural function of the knee. It is a paradigm shift from the current standard of care—reconstruction that replaces the ACL with a graft."

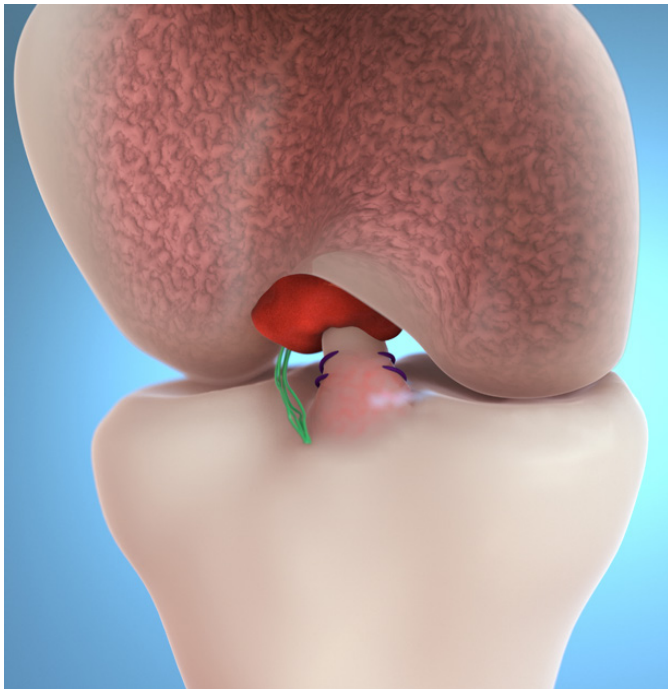
"The BEAR Implant is the first medical technology to demonstrate, with Level 1 clinical evidence, that it enables the body to heal its own torn ACL."

"Unlike reconstruction, which is the current standard of care, the BEAR Implant does not require a second surgical wound site to remove a healthy tendon from another part of the leg or the use of a donor tendon. Instead, it acts as a bridge to help the ends of the torn ACL heal together."

"The surgeon injects a small amount of the patient's own blood into the implant and attaches it between the torn ends of the ACL in a minimally invasive procedure. The combination of the BEAR Implant and the patient's blood enables the body to heal the torn ends of the ACL, bringing them back together while maintaining the ACL's original attachments to the femur and tibia. As the ACL heals, the BEAR Implant is resorbed by the body."

Interim Clinical Study Data Released

Miach also released interim clinical study data for the BEAR implant. Patrick McBrayer, company president and CEO told *OTW*, "At the Orthopaedic Summit Evolving Techniques Conference, Bridge Registry investigator Dr. Greg DiFelice of Hospital for Special Surgery provided a sneak peek at interim results, which showed consistent safety



The Bridge-Enhanced Anterior Cruciate Ligament Restoration (BEAR®) Implant / Source: Miach Orthopaedics, Inc.

outcomes regardless of procedure technique in the first 100 patients evaluated at one year. We expect more detailed Bridge Registry results to be presented at a medical meeting and published in 2025 and will share further details at that time."

"The Bridge Registry is the first study to assess real-world performance of the BEAR Implant, focusing on safety data across a variety of surgical techniques and at multiple centers. Outcomes measured include IKDC [International Knee Documentation Committee] subjective score, AP knee laxity measured by pivot shift and Lachman tests, adverse events, RSI [repetitive strain injuries] and KOOS [Knee Injury and Osteoarthritis Outcome Scores]."

"ACL reconstruction has been the gold standard for decades," said Scott A. Sigman, M.D., chief medical officer and founder of OrthoLazer Orthopedic Laser Centers, to *OTW*. "BEAR ACL technology stands out by allowing surgeons to repair the ACL with a higher rate of healing. The BEAR technology allows surgeons to unlock the biological healing potential of the human body."

"BEAR ACL restoration preserves the normal neuromuscular status of the ACL which translates into patients stating their knees feel more normal. This opens up a more beneficial patient postoperative recovery and outcome. In addition, preclinical studies demonstrated a reduction in post ACL surgery knee osteoarthritis. If this translates into the human clinical experience. this would open up long-term benefits for our patients and would be the holy grail of ACL surgery." — *EH*

Brad Niemann Named 4WEB Medical President

Frisco, Texas-based 4WEB Medical has appointed Brad Niemann as president.

An industry veteran, Niemann has over 20 years of experience in the medical

Brad Niemann / Source: 4WEB Medical

technology industry. Over the course of his career he has served as a business leader with a number of orthopedic and spine companies.

Most recently, Niemann served as CEO of Conventus Flower Orthopedics, a provider of foot and ankle surgical solutions. Prior to that, Niemann served as executive vice president for WellAir Solutions.

Niemann also spent nearly eight years with Orthofix and for nearly six years served as president of Global Spine for Orthofix International. Earlier in his career, Niemann held roles of increasing responsibility at Enovis (formerly DJO Global).

When discussing his decision to join 4WEB Medical, Niemann expressed excitement about his new role commenting, "I've watched and admired 4WEB Medical for years. I've always been impressed with the impact that the company has had on our industry. 4WEB was first to market with 3D printed implants and quite honestly broke down the doors that the rest of the industry is walking through now."

Niemann continued, "What I am really excited about is contributing to the mission of positively affecting the outcomes of people's lives through the development of the truss technology. I have firsthand experience seeing the positive reaction from the surgeon community that utilizes 4WEB's product offering. I am excited to partner with the entire 4WEB team to help drive the organization to greater success."

4WEB Medical is an orthopedic implant company focused on creating patient-specific solutions. Its proprietary truss implant platform is manufactured with 3D printing technology.

4WEB Medical CEO Jessee Hunt commented, "4WEB is excited to have Brad join the team and lead our organization through our next phase of growth. Since launching our Truss Implant Technology™ in 2012 we have put significant effort in defining the clinical benefits of the truss implant. We are currently finalizing several advanced studies that will further bolster the story and redefine the gold standard for orthopedic implants. We look forward to sharing this data with the industry in the near future."

Hunt continued, "Brad's proven leadership in commercial and operational roles, as well as extensive experience managing significant growth, will be invaluable to the company as 4WEB continues to develop and market its differentiated technology." — *KD*

LARGE JOINTS

10-Year Data: Socioeconomic Factors Affect TKA Outcomes

Where does your total knee patient live? Do they have a college degree, access to transportation, adequate housing? Researchers from multiple sites found that these factors DO affect total knee arthroplasty (TKA) outcomes.

The teams collected 10 years of retrospective socioeconomic data covering such factors as education and housing, and tested the prognostic implications of these data for patient outcomes.

Their study, "A Nationwide Analysis of the Impact of Socioeconomic Status on Complications and Health Care Utilizations After Total Knee Arthroplasty Using the Area Deprivation Index: Consideration of the Disadvantaged Patient," appears in the September 2024 edition of *The Journal of Arthroplasty.*

According to study co-author Nicolas Piuzzi, M.D., an orthopedic surgeon with Cleveland Clinic in Ohio, "Prior studies indicate that socioeconomic status can heavily influence health disparities, leading to varied postoperative results. Given our commitment to addressing these disparities and improving outcomes for all patient demographics, we designed this nationwide study to analyze how socioeconomic deprivation, as measured by the Area Deprivation Index, affects TKA outcomes across the United States."

The results of this study, said Piuzzi, support tailored interventions which address socioeconomically disadvantaged patients.

The research teams used the Area Deprivation Index which is a weighted index of 17 census-based markers of material deprivation and poverty. The higher the number, the more the disadvantage. That data was then compared to such outcome data as complications, emergency department utilizations, readmission rates, and 90-day costs.

The results of the study showed a clear pattern. "Patients from high Area Deprivation Index areas showed statistically significant increases in medical complications within 90 days post-TKA, including higher rates of respiratory failures, acute kidney injuries, and urinary tract infections, despite a slight decrease in readmission rates," said Dr. Piuzzi.

Source: Wikimedia Commons and Acabashi

"Emergency department utilization was also notably higher among these patients, indicating that socioeconomically deprived patients may rely more on emergency services post-surgery."

"Additionally, healthcare costs for patients from high Area Deprivation Index areas were over $2,500 greater than those from lower-risk areas, even when controlling for factors like age and comorbidity burden. These findings highlight the importance of addressing socioeconomic deprivation as a risk factor in clinical outcomes and cost management."

Interestingly, the team not only looked at patients within higher socioeconomic risk levels, but also patients "near" such neighborhoods. *OTW* asked Dr. Piuzzi about that: "This approach allows for a broader understanding of the effects of proximal socioeconomic deprivation on patient outcomes, as healthcare access, transportation, and social services in nearby areas may still significantly impact patients' health and postoperative recovery, even if they do not reside exclusively within those disadvantaged neighborhoods, supporting the idea that proximity to these areas can still capture socioeconomic factors impacting patient outcomes."

Regarding the choice of 17 census-based markers of material deprivation and poverty, Dr. Piuzzi told *OTW*, "The 17 markers representing various economic and social indicators included median income, educational attainment, employment levels, housing quality, and access to essential resources. While each marker provides insight into socioeconomic deprivation, factors like income, employment status, and education level are generally understood to influence healthcare access, continuity of care, and overall health outcomes. Although we can't pinpoint which specific markers are most critical from this study alone, these factors emcompassed by

Area Deprivation Index are considered important in predicting post-surgical recovery and may relate to complication risks."

OTW asked Dr. Piuzzi for his opinion regarding the "lowest hanging fruit" for employing these study results in a care setting. "Case managers could focus on improving access to basic resources and ensuring support for follow-up care post-surgery," Dr. Piuzzi said.

"Practical interventions such as arranging reliable transportation for follow-up appointments, coordinating home health services, or providing access to affordable post-discharge care can potentially reduce reliance on emergency services for minor issues."

"Additionally, patient education on managing postoperative symptoms and when to seek emergency department care versus alternative resources may further enhance outcomes and reduce unnecessary healthcare utilization."

Finally, Puizzi noted; "Future studies could benefit from a deeper dive into specific social determinants that most directly affect post-surgical outcomes and exploring how long-term health outcomes vary among patients in deprived versus non-deprived areas."

"A longitudinal analysis extending beyond 90 days would allow for insights into chronic complications and health service utilization trends. Additionally, interventions targeting high Area Deprivation Index patients' specific needs—such as personalized discharge planning, socioeconomically adjusted risk stratification models, and policies that incentivize hospitals to serve higher-risk populations—could further mitigate the disparities identified in this study." — *EH*

New Data for Novel Cell Based Bone Graft

A novel cell-based bone graft, one that is going through the rigorous FDA Biologic License Application (BLA) process, has reached an important milestone in its first in-human clinical trials.

The new product, NVDX3-CLN01, developed by Belgium-based NOVADIP Biosciences S.A., is a cell-based bone substitute for fracture healing indications. The company recently released interim results from its first-in-human clinical trial and reported that, at six months post-grafting surgery with NVDX3, S-rays demonstrated that 90% of patients reached or are steadily progressing towards complete bone healing.

"NVDX3 is an allogeneic cell-derived product made of mineral particles with a neo-synthetized matrix containing growth factors and miRNA involved in the bone healing," Denis Dufrane, M.D., Ph.D., company CEO told *OTW.*

"NVDX3 is derived from our 3-dimensional cell-based platform with adipose stem cells. Indeed, our platform already demonstrated its safety and efficacy with the autologous bone product NVD003, a first-in-class product dedicated to the treatment of critical size bone defects and to avoid amputation."

According to the company, NVDX3 is a new class of regenerative tissue products that accelerates bone healing in a single treatment for patients at high risk of nonunion due to co-morbidities (aging, diabetes, obesity, smoking, and other conditions) and medication use. Ten participants, aged 28 to 84 years old, were treated.

According to the company, all but one are progressing as expected clinically and factors such as age or sex did not have a statistically significant effect on outcomes. The company also reported that there were no safety concerns arising from their study.

OTW asked Dr. Dufrane to provide details regarding the lyophilized powder and he said, "NVDX3 is a bioactive powder with less than 5% of residual moisture for preservation at room temperature in the operating room; it is available 7/24 for the surgeon."

"The Biologics License Application is the regulatory pathway to demonstrate the safety and the efficacy of a drug. NVDX3 is the first and the only product to follow the Biologics License Application pathway in the orthopedic field to demonstrate its pharmacological activity and restore bone physiology."

The 12-month results of NVDX3-CLN01 are expected at the end of 2024. Going forward, says the company, the first Phase 2b will focus on multilevel cervical spine fusion. — *EH*

NOVADIP's 3M3 stem cell platform, NVDX3 / Source: NOVADIP Biosciences S.A.

TKA Study: Women Have More Pain, More Tolerance?

To what extent does the sex of a patient influence pain perception?

A team from Northwell Health in New York organized a study to test the hypothesis that women experience more pain than men after total knee arthroplasty (TKA).

Their work, "One Size Does Not Fit All: Women Experience More Pain Than Men After Total Knee Arthroplasty," appears in the September 2024 issue of *The Journal of Arthroplasty.*

Co-author Jonathan R. Danoff, M.D., chief of adult reconstruction at North Shore University Hospital, told *OTW*, "I have led collaborative efforts in my health system at Northwell Health, amongst the hip and knee arthroplasty surgeons, anesthesiologists, and other physicians, to standardize perioperative care for our primary total joint replacement patients. We created a standardized preoperative, intraoperative, and postoperative pain regimen for all patients, but I noticed that various groups of patients, such as the men and women, would complain of pain differently and have different pain medication requirements."

"Simultaneously, in the non-orthopedic literature, there has been significant interest in the fact that men and women and patients of various ethnic backgrounds may respond to medications differently, and I began to wonder whether it makes sense that we treat all populations of patients the same, with exactly the same pain medication protocol regardless of age, sex, race, or ethnicity. Possibly, certain patients would be more sensitive to medications and others less sensitive."

Also associate medical director of the Schwartz Ambulatory Surgery Center, Dr. Danoff explained, "There was no literature specifically comparing men and women in arthroplasty from a pain perspective, and so this was the first study to be published to assess whether men and women experience pain differently after total knee replacement surgery."

Methodology

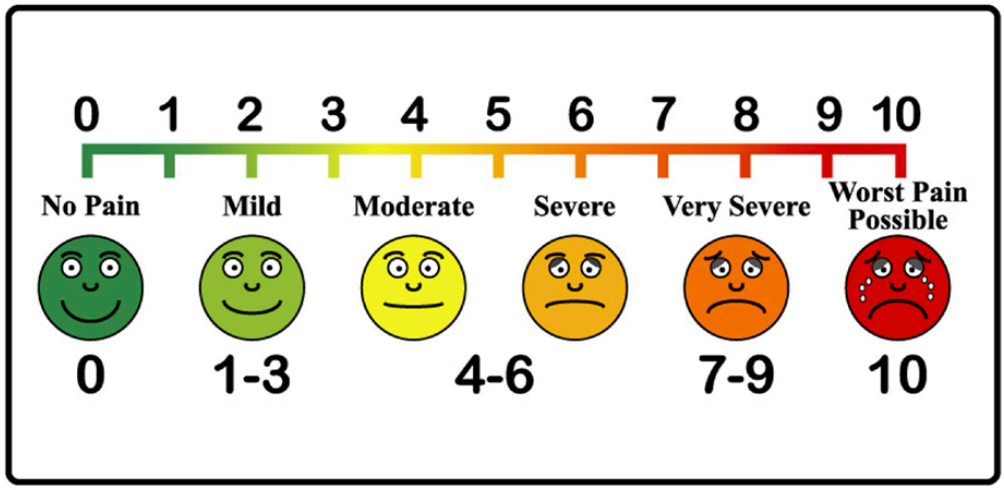
The researchers prospectively collected Visual Analog Scales (VAS) and Knee Injury and Osteoarthritis Outcome Junior scores for 150 patients (64 men and 86 women). They recorded each patient's:

- mean pain scores,
- delta pain scores,
- time to achieve minimal clinically important differences,
- influence of pregabalin (Lyrica), and
- opioid consumption at
  - o baseline,
  - o day of surgery,
  - o 24 hours,
  - o 48 hours, and
  - o 72 hours postoperatively,
  - o as well as postoperatively weeks 1, 2, 6, 12, and 26, and
- compared between women and men cohorts.

Results

"Interestingly," said Dr. Danoff to *OTW*, "we found that women did report experiencing significantly more pain than men at all time points postoperatively (through six months) at rest and when walking, although they did not require higher levels of narcotics than men."

"Essentially, women seem to have more 'grit' than men which was very interesting. Simultaneously, in parallel, we tried to assess whether Lyrica (pregaba-



Source: FreeSVG.org

lin) would have an influence on patient pain, and we did not find that there was any benefit to use of this medication for either group."

Higher VAS Pain Scores for Women at All Time Points

The Visual Analog Scales pain scores for women were higher than for men at all study time points. The change in Visual Analog Scales walking and mean Knee Injury and Osteoarthritis Outcome Junior scores from baseline to final follow-up at 26 weeks were not significantly different between cohorts. Both cohorts achieved Visual Analog Scales minimal clinically important difference by two weeks postoperatively.

No significant differences in opioid consumption between men and women were noted during the study time periods. Women were also noted to have significantly higher raw Knee Injury and Osteoarthritis Outcome Junior scores than men at all-time points, except for at 26 weeks postoperatively. Interim analysis revealed no significant influence of pregabalin on Visual Analog Scales scores, so this arm of the study was discontinued.

"Given the results of our study," said Dr. Danoff, "we eliminated pregabalin from our multimodal pain regimen at our hospital and we do not recommend surgeons use this medication after total knee arthroplasty for pain control."

"It is imperative that we perform further studies extrapolating from the results of this study to see how we can better customize our perioperative protocols to make them unique to each population of patients that we treat to best serve our patients. A one-size-fits-all model for our multimodal pain regimens should be reconsidered." — *EH*

SPINE

How Much Does BMI Affect MIS-TLIF Outcomes?

Answer: Significantly. Here are the details.

A research team from both the U.S. and Germany set out to calculate and quantify the effect of a high BMI (body mass index, >35) on minimally invasive transforaminal lumbar interbody fusion (TLIF) outcomes. Their work, "Class 2/3 obesity leads to significantly worse outcomes following minimally invasive transforaminal lumbar interbody fusion," was published in the September 2024 edition of *The Spine Journal.*

"Minimally invasive spine surgery [MISS] is increasingly being utilized and offers benefits such as less postoperative pain, shorter hospital stay, and faster recovery," said co-author Pratyush Shahi, M.B.B.S., M.S.(Ortho) to *OTW.*

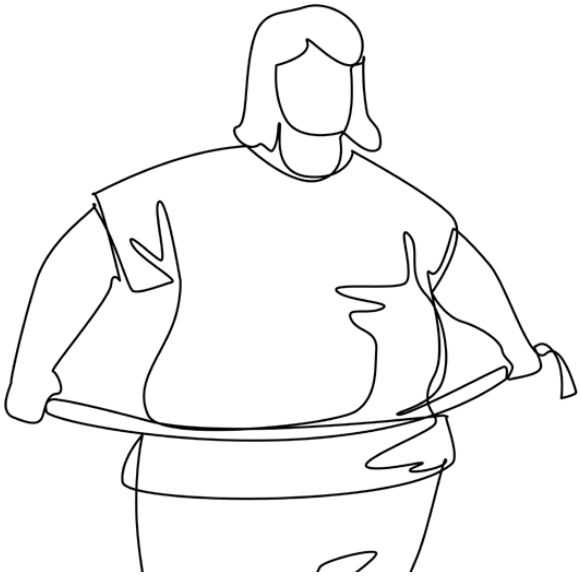
A past minimally invasive spine surgery research fellow at Hospital for Special Surgery in New York, Dr. Shahi explained, "Obese patients form a significant subset of patients undergoing spine surgery. However, there is little evidence on how obesity, especially class 2/3 obesity defined as a body mass index >35, impacts outcomes after surgery."

"The purpose of this study was, therefore, to analyze clinical outcomes, return to activities, fusion rates, and complication/reoperation rates following minimally invasive transforaminal lumbar interbody fusion (minimally invasive spine surgery - transforaminal lumbar interbody fusion) in class 2/3 obese patients and compare them with the other body mass index groups."

Methodology

The researchers divided 390 patients into four groups based on their body mass index:

- normal (18.5 to <25),
- overweight (25 to <30),



Source: Shutterstock

- class 1 obesity (30 to <35), and
- class 2/3 obesity (BMI >35).

There were 119 patients in the normal body mass index group, 160 who were overweight, 67 in the class 1 obesity group, and 44 with class 2/3 obesity.

Under 6 Months, Little Difference. More Than 6 Months, Big Difference

Although no significant difference was seen between the groups in patient reported outcome measures at less than 6 months, at more than 6 months, the 2/3 obesity patients reported significantly worse outcomes, lower patient acceptable symptomatic state achievement rates, and lower minimal clinically important difference achievement rates in Visual Analog Score leg and Short Form-12 Physical Component Summary.

Other study findings were:

- No significant differences in the minimal clinically important difference achievement rates in the Oswestry Disability Index and Visual Analog Scores (back) and responses on the Global Rating of Change scale.
- The class 2/3 obesity group had a lower fusion rate (67% vs. >87% in other groups), but it was not statistically significant.
- The class 2/3 obesity group had significantly higher postoperative length of stay (62 hours vs. <50 hours in other groups) and
- Took significantly greater number of days to return to driving (74 days vs. <40 days in other groups).
- No significant difference was found in return to work and discontinuation of narcotics. The groups had similar complication and reoperation rates.

A minimally invasive and endoscopic spine surgery fellow at Wooridul Spine Hospital in Seoul, South Korea, Dr. Shahi told *OTW,* "We found that although class 2/3 obese patients showed significant clinical improvement following minimally invasive spine surgery - transforaminal lumbar interbody fusion, the magnitude of improvement was less compared to the other body mass index groups. They also took longer to be discharged from the hospital and return to driving following surgery. No significant difference was seen in fusion rates and complication/reoperation rates."

"The findings of the study suggest that morbidly obese patients are likely to have poorer outcomes and slower recovery compared to other body mass index groups after minimally invasive spine surgery—transforaminal lumbar interbody fusion," stated Dr. Shahi to *OTW.*

"This does not preclude these patients from undergoing minimally invasive spine surgery - transforaminal lumbar interbody fusion as they still improve significantly compared to before surgery, but this highlights the possible need of preoperative optimization through weight loss for better outcomes."

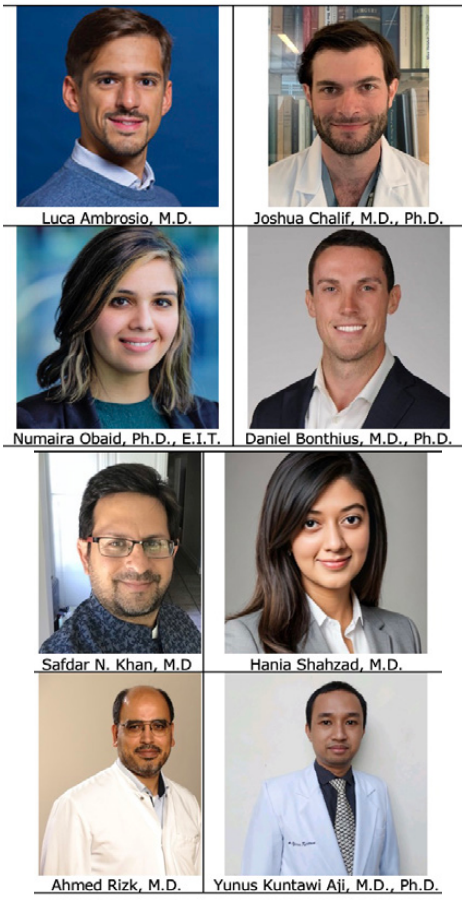
"These findings can help in preoperative patient education, setting of realistic expectations, and shared decision-making. The study also lays the background for future cohort studies to analyze the impact of preoperative optimization of obesity on clinical outcomes after elective spine surgery." — *EH*

PEOPLE

NASS Awards $159,059 in Grants, Fellowships to Spine Researchers

At its recently concluded annual meeting the North American Spine Society (NASS) announced the 2024 Research Funding Program winners. These grants and traveling fellowships, which total $159,059 this year, provide funding for promising projects by qualified investigators in spine care.

The recipients were selected by the NASS Research Funding Commit-



Images courtesy of LinkedIn

tee and Evidence Analysis & Research Council, and approved by the NASS Executive Committee based on scientific merit, significance of the project, approach, and feasibility.

The 2024 Research Funding Recipients are:

Grant (Young Investigator – Basic)

- Study Title: "Extracellular Vesicles Derived from Tie2-enhanced Nucleus Pulposus Progenitor Cells: An Innovative Cell-free Therapy for Intervertebral Disc Degeneration"
- Principal Investigator: Luca Ambrosio, M.D.
- Amount: $20,000

Dr. Ambrosio told *OTW,* "This project aims to explore the regenerative potential of nucleus pulposus cells (NPCs) specifically overexpressing the Tie2 receptor, which has been associated with a biologically potent progenitor phenotype. Extracellular vesicles isolated from such cells will be investigated as an innovative regenerative therapy for intervertebral disc degeneration both in vitro and in vivo using a large animal model."

Grant (Basic)

- Study Title: "Manipulating Ventral Spinocerebellar Tract Neurons for Promoting Functional Recovery after Spinal Cord Injury"
- Principal Investigator: Joshua Chalif, M.D., Ph.D.
- Amount: $40,000

"Ventral spinocerebellar tract neurons have recently been discovered to be essential in mammalian locomotion," commented Dr. Chalif to *OTW.* "The current proposal plans to explore how activation of VSCTs may provide improvement in locomotor ability following spinal cord injury."

Grant (Clinical)

- Study Title: "Improving Patient Health Literacy through Gamification of Medicine using Augmented Reality-Powered Tools for Common Spinal Conditions: A Proof-of-Concept Study"
- Principal Investigators: Safdar N. Khan, M.D. and Hania Shahzad, M.D.
- Amount: $13,000

The authors told *OTW*, "This study aims to utilize augmented reality models accessible on a user's personal device (surgeon/resident/patient) to enhance patients' health literacy about their spinal disease and treatment. The goal is to support patient-centric efforts and foster health care decision-making driven by patients themselves."

Grant (Clinical)

- Study Title: "Examining CSF Hydrodynamic Changes in Stenotic Patients Using 4D Flow MRI"
- Principal Investigator: Numaira Obaid, Ph.D., E.I.T.
- Amount: $25,059

"Degenerative stenosis in the cervical spine is a prevalent problem in older adults, causing adverse impacts on the central nervous system," noted Dr. Obaid to *OTW*. "Stenotic obstruction of the cerebrospinal fluid can reduce cord protection, and we aim to systemically investigate the effect of degenerative stenosis on local CSF flow and its influence on the spinal cord."

Grant (Young Investigator – Translational)

- Study Title: "Rib Fixation for Prevention of Proximal Junctional Kyphosis (PJK) in Adult Spinal Deformity Surgery"
- Principal Investigator: Daniel Bonthius, M.D., Ph.D.
- Amount: $40,000

Dr. Bonthius told *OTW*, "Proximal junctional kyphosis (PJK) is an important problem following adult spinal deformity surgery. The proposed studies will explore a new method of PJK prophylaxis that utilizes rib fixation to create a "soft landing" at the upper instrument vertebrae (UIV) in high-risk patients undergoing fusion surgery for spinal deformity."

Fellowship (Clinical Traveling Fellowship)

- Award Recipient: Ahmed Rizk, M.D.
- Participating Institutions: Barrow Neurological Institute, Swedish Medical Center, Inspired Spine Health, Duke Health System
- Amount: $7,000

Dr. Rizk told *OTW,* "I will focus on expanding my knowledge in performing endoscopic spinal surgeries, including endoscopic-TLIF surgeries; minimally invasive lateral procedures including Lateral Lumbar Interbody Fusion (LLIF)/Oblique Interbody

Fusion; degenerative deformity corrective procedures involving LLIF, Anterior Lumbar Interbody Fusion, Transforaminal Lumbar Interbody Fusion; and spinal tumor procedures like corpectomy. Though I have completed coursework involving cadaveric workshops for most of these procedures, this opportunity will provide invalulable insight and training on technical operative details and decision-making that will allow me to help more patients, as well as improve the quality of service given."

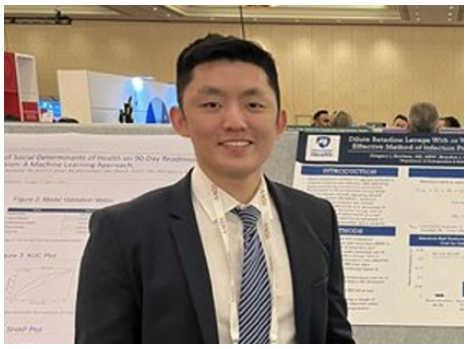
Fellowship (Clinical Traveling Fellowship)

- Award Recipient: Yunus Kuntawi Aji, M.D., Ph.D.
- Participating Institutions: Technical University of Munich (Germany), Yonsei University Health System (S. Korea), Korea University College of Medicine (S. Korea)
- Amount: $7,000

"By pursuing this fellowship," stated Dr. Aji to *OTW*, "I hope to learn about endoscopic surgical techniques, including advanced procedures in endoscopic decompression, discectomy, and fusion, as well as enhance my understanding of patient selection criteria and preoperative planning for endoscopic procedures. Ultimately, my goal is to become a leader in the field of minimally invasive spine surgery in Indonesia, advocating for the adoption of advanced techniques and improving patient outcomes. Upon completion of the fellowship, I am committed to returning to Indonesia and sharing my knowledge and expertise with colleagues at the National Brain Center Hospital in Jakarta, thereby enhancing the quality of spine care in my country." — *EH*

Andrew Kim Wins Best Paper at 2024 NASS

Andrew Kim, B.S. was honored with a "Best Paper" at the recent North American Spine Society (NASS) meeting in Chicago. His work (publication in progress), is titled, "Neurologic Adverse Events Following Three-Column Osteotomy: A Prospective Multicenter Study."



Source: Andrew Kim

In the first study to compare sensory and motor complications between adult spinal deformity patients with and without three-column osteotomies, Kim and his colleagues looked at 553 adult spinal deformity patients who underwent this surgery. Those with and without three-column osteotomies were compared with respect to patient demographics, surgical characteristics, and neurologic complications.

"In adult spinal deformity surgery, three-column osteotomies are often used to correct severe/rigid deformities," said Kim to *OTW*. "Current literature has found an association between three-column osteotomies and high complication rates, with variable impact on postoperative neurologic outcomes. Thus, our research study aimed to identify the rate of neurologic complications following adult spinal deformity surgery and characterize the differences in incidence between patients with and without three-column osteotomy."

"In our study," explained Kim to *OTW*, "we found that adult spinal deformity patients who underwent three-column osteotomy were:

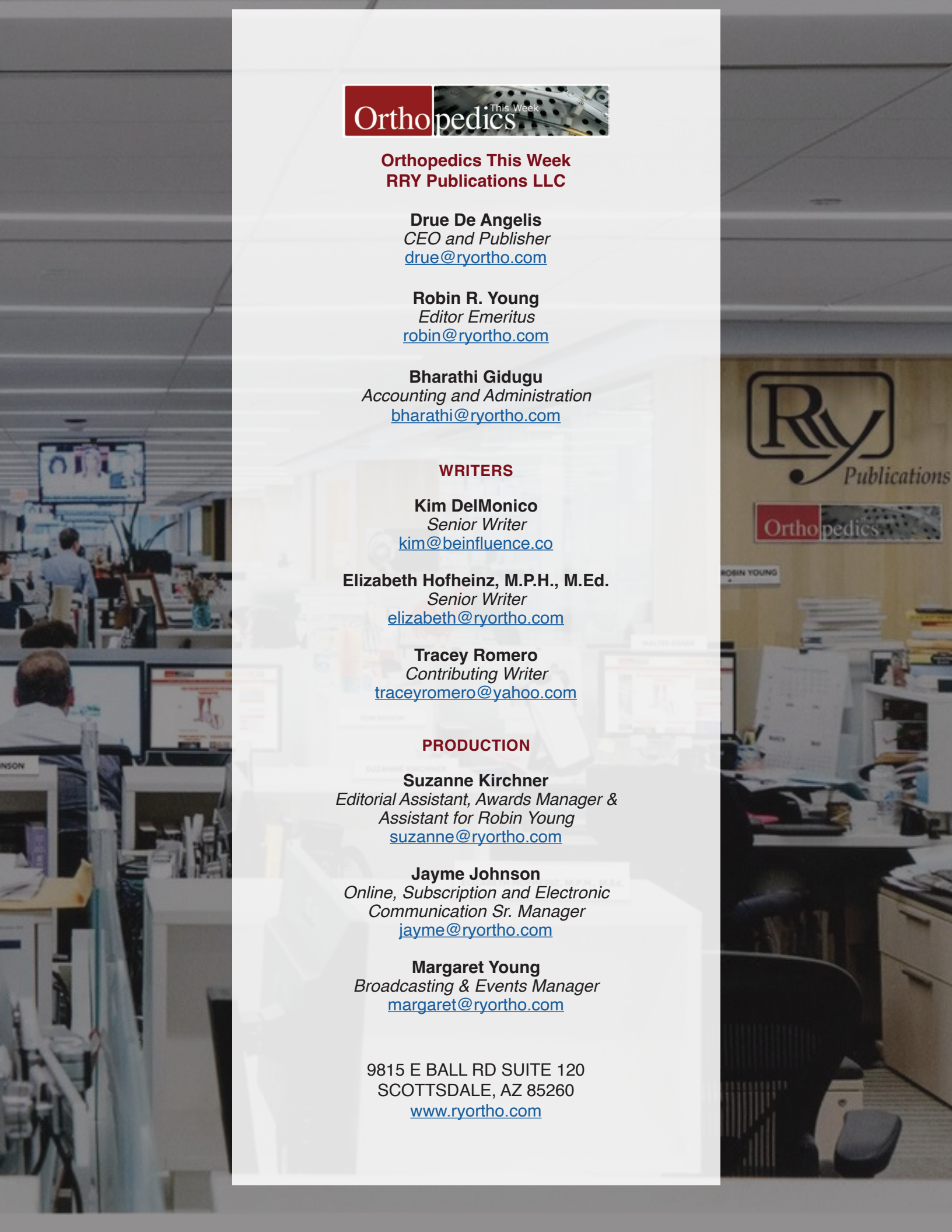
- more likely to be revision patients (67.7% vs. 35.0%),
- present with sagittal deformity (43.9% vs. 31.0%), and
- have greater operating room time (455.6 vs. 407.2 minutes) and
- have estimated blood loss (1,971.2 vs. 1,286.2 cc) compared to those without three-column osteotomy.

Additionally, there was a greater overall incidence of early postoperative adverse neurologic events in patients who underwent three-column osteotomy compared to patients without three-column osteotomy."

"Interestingly, there was no difference in lower extremity motor strength at 1-year follow-up or 1-year change from baseline between adult spinal deformity patients with and without three-column osteotomy."

Importantly, said Dr. Kim, among adult spinal deformity patients, risk of complication should not be considered a contraindication when deciding whether to perform three-column osteotomy … or not.

"Our study demonstrates there was no change in lower extremity motor strength or neurologic deficits at 1-year follow-up. Surgeons should choose the procedure they feel is best in correcting a patient's spinal deformity based on surgeon experience and individual patient risk profile." — *EH*



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