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Risk stratification is not a "universal language", numerous IMAST presentations find

The benefits and challenges of risk stratification research in spinal surgery were explored in detail during the 2016 International Meeting on Advanced Spinal Techniques (IMAST; 13-16 July, Washington, DC, USA) with presenters noting again and again the difficulties in translating "big data" conclusions into good clinical outcomes. The potential yield of such data was generally agreed to be significant, across talks focusing on its impact on spinal surgery in individual countries, on payers and on patients themselves. The challenges of maximising these datasets across different countries—and even smaller regions—with different default treatment strategies, different payment systems, and different access to healthcare, were shown to be daunting—but not necessarily insurmountable.

Steven Glassman (Louisville, USA) presented the results of his team's efforts to combine risk stratification models from Denmark (DaneSpine), the USA (N2QOD) and Japan (JMSD), asking the question, "Is risk stratification a universal language?" Glassman asserted that by pooling different datasets, researchers might be able to address the different levels of granularity and generalisability found in administrative, society-based and study group data.

Characterising risk stratification as "Identifying demographic characteristics and co-morbidities that are likely to predict complications and clinical outcomes", Glassman noted, "Although it sounds as though it would be complicated…it is what we do every day in the office when we look at a patient." It will be "key" in the assessment of patients, and in decision-making, Glassman said.

The three nationwide databases chosen were assessed for predictors of hospital readmission and surgical site infection. The research team initially tried to pool the three registries, in an attempt to assess the feasibility of combining local data into a useful global dataset. Whilst there was a reasonable amount of overlap between the three registries, they had all collected slightly different sets of variables. Results were compared for 30-day readmission rates and surgical site infection, with each database revealing different predictive factors. The US database found American Society of Anesthesiologists grades to be predictive of readmission, with gender and the number of levels fused predictive in the Japanese and Danish registries, respectively. For surgical site infection, only the Japanese database revealed predictive factors; gender, diabetes and length of stay. When data were pooled, the biggest predictive factor for 30-day readmission was in fact which database an individual appeared in (p=0),

Rajiv Sethi

Steven Glassman

with gender (p=0.011) and employment (p=0.03) following. Similarly, the researchers found a paucity of significantly predictive factors for surgical site infection, with database (p=0), length of stay (p=0), gender (p=0.001) and body mass index (p=0.001) the strongest predictors.

Glassman cautioned against pooling international data, and even national data in countries with a low level of population homogeneity—such as the USA. A subtle approach is needed, rather than simple aggregation, he claimed, stating, "Differences in the underlying cohort seem to outweigh the individual patient variables or drivers of risk." He advised, "We probably need to have more consensus on diagnosis, more uniform demographic data, and probably a core set of outcome measures," concluding that "risk stratification models from one country just may not be applicable to other countries."

The importance of maximising these kinds of registry was the focus of a number of talks during IMAST's "Modern Perspectives on Spine Care" session. Benny Dahl (Copenhagen, Denmark) detailed his successful experiences with the Spine Adverse Events Severity System (SAVES; for

The best predictor of readmission was **which database** a patient appeared in

recent results of Dahl and colleagues' work, see *SNI* 38, p11). Calling "big data", "the future", he emphasised the importance of collecting "non-surgical" patient outcomes data alongside clinical and radiographic records in complex patient populations. "At least in our healthcare system," Dahl said, "there is a high focus on transparency of outcomes—not only related to mortality, but to healthcare-related quality of life". A big challenge for physicians practicing this kind of registry-building is who has control over results data, Dahl claimed, saying, "We will have to be very, very specific regarding risk stratification when reporting these data—and be ready to read the criticism of some of our treatment results." This concern echoed a potential benefit described by Glassman, who had said of proper risk stratification reporting, "It is a way to level the playing field, so that the doctors doing very hard cases are not compared head-to-head with doctors who would only be doing simple cases."

Rajiv Sethi (Seattle, USA), another symposium presenter, queried the applicability of risk stratification efforts like SAVES, to multiple-payer regions like the USA, "with different parameters" for success. Dahl responded by saying "I do not think you are doomed." He emphasised that transparency extended beyond national single-payer systems, and that "input from different payer systems" may require different methods of treating data. Successful transformation of "big data" into hard results on an international scale remains elusive.

Two further presentations at the session queried the ability of risk stratification data to help navigate healthcare in value-based systems. Marinus DeKleuver (Amsterdam, the Netherlands), concentrating on spine problems in the elderly, emphasised the importance of making sure that

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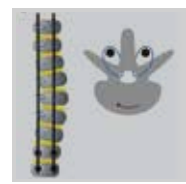

UHMWPE cables: Feature **Page 12**

Posterior BMP-2 use does not lead to increased cervical deformity surgery-related complications

Whilst a number of studies have assessed the incidence of complications in association with posterior BMP-2 (bone morphogenetic protein-2) use, researchers from the International Spine Study Group noted that none focus on cervical deformity. Presented by Han Jo Kim at the 23rd International Meeting on Advanced Spinal Techniques, a new study from the group has found no significant increase in complications associated in cervical deformity surgery with posterior BMP-2, as compared to surgery without BMP.

Kim explained the importance of studying BMP-2 use in cervical deformity surgery, "Where fusions are crossing the cervicothoracic junction more frequently, where instrumentation is smaller and [where] biologic time to fusion is unchanged, you could argue that BMP use could be beneficial to allow for earlier fusions, and for maintenance of correction." Studying the safety of such usage, thus, is paramount to make sure that patients can receive the best care in these cases.

Using data from a prospective cervical deformity database from 2013–15, the researchers selected 100 patients matching at least one of their inclusion criteria; cervical kyphosis or scoliosis greater than 10 degrees, C2–7 sagittal vertical axis greater than four degrees, or horizontal gaze impairment with a chin-brow vertical angle greater than 25 degrees. Within this population, data from 53 patients who had been treated using BMP-2 were compared with data from 47 patients with no BMP-2 usage, by linear regression analysis

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Development of radiopaque UHWMPE

From idea to 510k approval

Chris Arts and colleagues at Maastricht University Medical Centre (Maastricht, the Netherlands) have developed and tested innovative radiopaque ultra-high molecular weight polyethylene (UHWMPE) wires for the treatment of early onset scoliosis. Intended to eliminate revision surgeries associated with treatment of the condition, Arts *et al* believe that adoption of the technology could drastically reduce costs for institutions, and lessen the psychosocial burden of multiple surgeries on patients. Their project is part of a collaboration between private industry, the government of the Netherlands, and a number of Dutch universities. In this special feature for *Spinal News International*, they describe the process of developing the technology, the journey to US Food and Drug Administration (FDA) 510(k) approval, and their hopes for the future adoption of UHWMPE cables.

Early onset scoliosis is a complex 3D spinal deformity with an overall prevalence of 2-3%.[1] The trunk becomes deviated from its normal plane of symmetry, inducing a lateral curvature and rotation of the vertebrae. Deformities of the spinal column can severely limit patient activity, compromising life expectancy and quality.[2] Early onset scoliosis is a common disease with an overall prevalence of 0.47–5.2% in the current literature.[3] The female-to-male ratio of patients ranges from 1.5:1 to 3:1, increasing substantially with age. Method of treatment is based on age, curve magnitude and risk of progression, and aims to keep curves under 50° at maturity. Treatment options for progressive idiopathic scoliosis in a growing child are limited to:

1. **Observation:** Recommended for immature patients with spinal deformity curves of less than 25°.
2. **Orthotic bracing:** Recommended for immature patients with progressing spinal deformity curves between 25° and 50°.
3. **Surgery:** Recommended if the spinal deformity has a curve of 40° to 50°, or when swift curvature progression is evident.

Standard surgical treatment of early onset scoliosis

Surgical treatment of early onset scoliosis is challenging due to the incomplete development of both the spine and thoracic cavity. Spinal fusion in young patients can result in a halt to spinal development, and thoracic cavity size and growth, with a subsequent detrimental effect on lung development.[4,5] Underdevelopment of the lungs may ultimately lead to lung insufficiency syndrome, and is associated with increased morbidity and mortality.[5] Current treatment methods for early onset scoliosis therefore rely on periodical surgical procedures to lengthen the implanted posterior metal rods. Such surgical procedures are risky for patients due to comorbidities, are associated with high costs, and can negatively affect patient quality of life. Although spinal correction is achieved through surgery, serious limitations on both materials and correction procedures prevent optimal deformity correction in adolescent patients.[6,7]

Titanium cables and laminar wires have elastic behaviour that may result in cable fracture, offering less than optimal strength. These cables and wires also have a tendency to grind into the bony structure of the spine. Another major setback is the inability to repeatedly adjust cable tension during surgery.

Correction for rotational deformity is procedurally very difficult. Moreover, loss of correction over time with laminar wiring systems is a reported clinical problem. Conventional growing rods still require surgical lengthening procedures at six-to-eight month intervals. This places a huge physical and psychosocial burden on patients, while generating enormous healthcare costs. Furthermore, a definitive fusion procedure will be required upon reaching skeletal maturity.

BMM Spineguide project

In 2008, the Ministry of Economic Affairs in the Netherlands started a public-private funding scheme entitled BMM (BioMedical Materials) with a budget of €90m. One of the supported projects, BMM Spineguide, was a cooperation between DSM Biomedical, Eindhoven University of Technology, Maastricht University Medical Centre and Twente University, all based in the Netherlands. A new growth-guidance system and surgical technique for the treatment of early onset scoliosis was developed through BMM Spineguide between 2010 and 2014, using a construction of metal rods and constructions made with Dyneema Purity fibres. The system is intended to provide 3D deformity correction over time, whilst preserving spinal mobility and allowing for growth.

Conceptually, placing an "internal brace" (Figure 1) in the form of a metal rod linked to a construction of radiopaque UHMWPE sublaminar wires (Dyneema Purity, DSM) per spinal level would allow the spine to grow longitudinally in a growth guidance construct while also maintaining curve correction. After completion of growth or adequate curve correction, removal of the implanted devices should yield a flexible spine with reduced deformity.

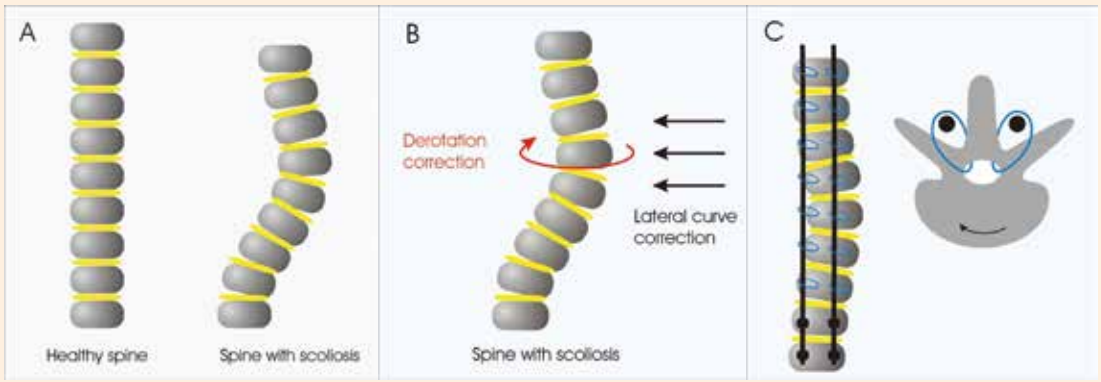

Figure 1 **[A]**: Schematic dorso-ventral view of a healthy and right convex scoliotic spine. **[B]**: Schematic overview of 3D correction mechanisms in idiopathic scoliosis; distraction in the concave area will result in correction of the frontal curve. Red arrow indicates the rotational correction. Black arrows indicate the translation correction. **[C]**: Proposed clinical solution in adolescent EOS patients: posterior approach showing metal rods (black) placed in a longitudinal direction along the spine and fixed with pedicle screws (red arrows) as well as radiopaque UHMWPE cables (blue) per vertebral body segment.

Radiopaque ultra-high molecular weight polyethylene

Our team replaced metal sublaminar wires with UHMWPE wires. Due to the smooth surface properties of their fibres, it was hypothesised that superior growth results could be attained with the cables, as compared to metal wires. Other shortcomings of metal wires—such as the inability for re-tensioning and the occurrence of damage to soft tissues during wire changes—would also be addressed. Radiopaque UHMWPE sublaminar wires can be used to fix the affected vertebrae within the deformity to a posterior metal rod.

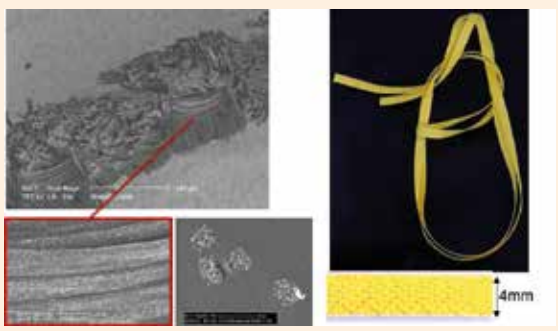

Figure 2 **[Right]**: 4mm-wide radiopaque UHMWPE sublaminar wire and the double-loop sliding knot with extra pass used to secure the wire. **[Left]**: Scanning Electron Microscope clearly show homogeneous distribution of Bismuth Tri-oxide (20% weight addition) particles used as radiopacifier.

Roadmap to 510(k) approval

The FDA granted 510(k) clearance for the radiopaque UHMWPE sublaminar wires in 2015, following extensive testing to determine strength, growth allowance, biocompatibility and optimal surgical technique.

Strength

The novel radiopaque UHMWPE sublaminar wires were extensively tested and compared to titanium sublaminar wires (Atlas, Medtronic). Results indicated that the coefficient of friction between a rod and UHMWPE cables is indeed lower than that between a rod and metal cables. Subsequently, in both mechanical test and animal models we have proven that the combination of metal rods and constructions made with Dyneema Purity fibres are able to allow longitudinal growth.

Optimal knotting technique, tensile strength, fatigue strength, wear particle accumulation and performance of instrumentation in animal cadaveric spine segments have all been determined by earlier *in vitro* tests.[11] Dynamic tensile fatigue testing on UHMWPE sublaminar wires—including knotting technique—revealed a fatigue strength far superior to other sublaminar wires (1550N, run-out five million cycles, as compared to 300N or less for metal wires). Increased fatigue strength allows a reduced number of levels to be instrumented without compromise to the long-term integrity of the sublaminar wires. Compared to the titanium cables used earlier, these UHMWPE cables offer lower friction, increased tensile strength and superior fatigue strength.

Growth allowance

Due to the smooth-surface properties of the UHMPWE wire and low coefficient of friction, sliding of the wires along the rods is possible, thus allowing for longitudinal growth. Proof of longitudinal growth allowance was established in two animal studies (Figure 3).[8,9]

sublaminar cables for early onset scoliosis

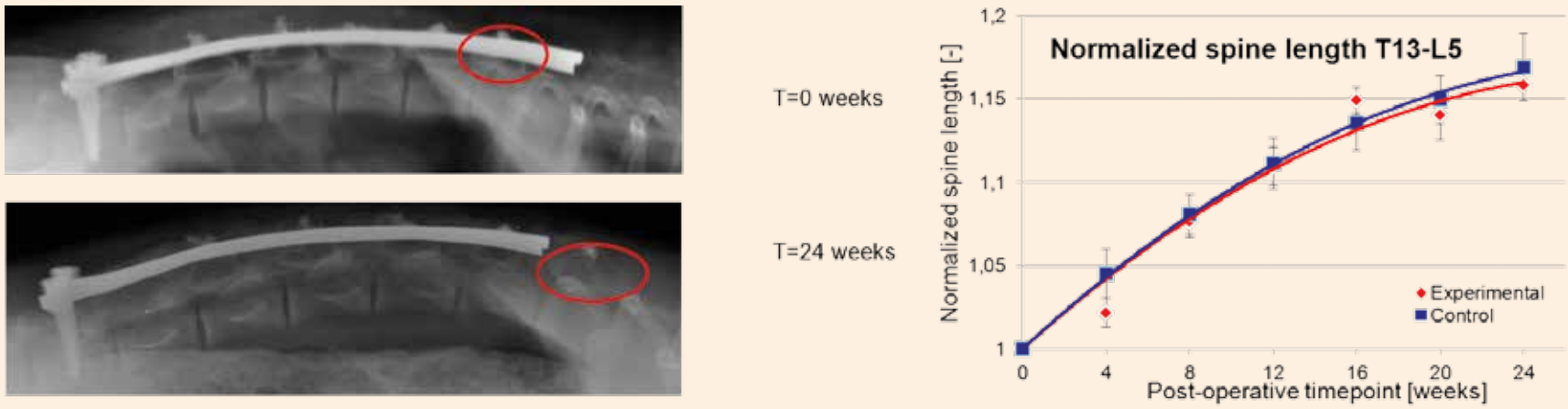

Figure 3 **[Top]:** Direct postoperative (upper) and 24-week postoperative lateral radiograph (lower) of the instrumented sheep spine. Marked growth of the instrumented segment has occurred as illustrated by sliding of the most cranial UHMWPE sublaminar wire (red circle). Novel radiopaque UHMWPE sublaminar wires are clearly visible on radiography (arrows). **[Bottom]:** Average growth (cm) and standard deviation values of the experimental group and control group. Both curves show a similar pattern with cessation of growth after 24 weeks.[9]

Biocompatibility

The wires were tested *in vivo* for the first time in animal models. Since the wires are visible on X-rays, it was possible to assess the status and position. Biosafety assessment entailing biocompatibility, toxicology and oxidation has been demonstrated *in vivo* and resulted in excellent biocompatibility (Figure 4). Barely detectable levels of bismuth trioxide have been observed in the liver and kidneys, but none has been found in the tissue surrounding cable placement.[8,9]

Surgical technique

The optimal number of consecutive levels instrumented with the UHMWPE sublaminar wires was determined in a biomechanical test setup, in which the range of motion in flexion/extension, side bending and axial rotation can be determined. Based on results in both flexion/extension and side bending, it appears that instrumentation with UHMWPE is optimal at two consecutive end levels. Instrumenting more consecutive end levels with the wires does not seem to be beneficial in terms of providing additional spinal stabilisation. However, growth needs to be anticipated for early onset scoliosis patients.

Dependent on the patients' age and expected remaining growth, extra rod length—or perhaps an extra end level—should be instrumented, so that two end levels remain instrumented even in the case that the UHMWPE wires slide off the rod at the most distal or proximal points.

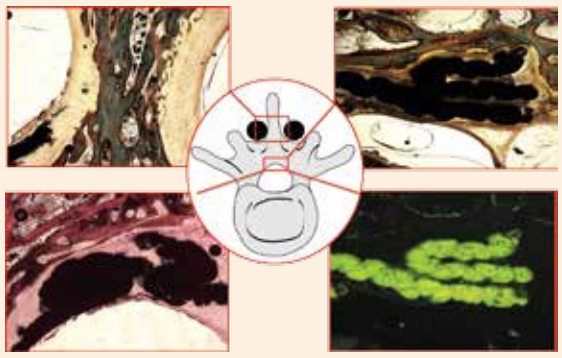

Figure 4: Histology assessment after 24 months *in vivo* using Mason Goldner stains (Top left and right), HE stain (down left and polarised light (down right) showing fibrous tissue encapsulation of the UHMWPE cable without foreign body giant cells or signs of inflammation. No fragmentation of UHMWPE cable was observed.[8-9]

Figure 5: Four-point bending test setup for the application of flexion/extension, lateral bending, and axial rotation to multilevel spinal segments. A standard material-testing machine applied load to the point indicated by the arrow for flexion/extension and lateral bending, while the circular arrows represent the pivot points. For lateral bending, the spine segment was rotated 90°. For axial rotation, torque was applied using a metal wire to the left cup. Light-emitting diode markers were fixed to each vertebral body, and were tracked using a 3D motion-capturing system.[11]

The safety of surgery using UHMWPE wires is also potentially improved, as it eliminates the sharp edges of broken metal wires that can harm the patient or surgeon, potentially providing safer surgical procedures.

Potential economic savings of the procedure

It is hoped that this new surgical instrumentation technique will provide a one-step surgical scoliosis treatment option—able to preserve 3D deformity correction, longitudinal spinal growth and spinal mobility, without the need for revision surgery. This should dramatically reduce the number of periodic surgical procedures.

As a majority of early onset scoliosis cases are of neuromuscular origin, minimising the number of procedures per patient is of great interest; overall health and quality of life can be improved for these patients, while total healthcare costs can be reduced.

Use of this technology could reduce the amount of revision surgeries needed to allow longitudinal spinal growth from five to one, freeing up four surgery slots. Considering the cost of a single early onset scoliosis surgery and rehabilitation is estimated to be between €47,000 and €65,000 in the Netherlands, total treatment costs could be reduced by €200,000 per patient. In the USA, estimated costs of the primary surgery average US$103,143, with and total—potentially avoidable— readmission costs averaging US$67,262 per patient.[10] Furthermore, this reduction in surgeries could also reduce additional healthcare consumption for physiotherapy and pain medication. These advantages should result in a fast implementation of this surgical technique, both inside and outside the Netherlands.

Although the present proposal focuses on the application for early onset scoliosis, we expect that there will be widespread clinical applications that could include restoration of vertebral deformation in osteoporotic patients and in spinal fusion procedures.

Approximately 38,000 scoliosis patients undergo a surgical correction procedure annually in the USA. Of these patients, approximately 2.5% suffer from neuromuscular disease. The neuromuscular-type scoliosis patient group would benefit most from this novel surgical technique, but the much larger groups of scoliosis and osteoporotic (50% of all females, 15% of all males) patients undergoing spinal fusion procedures (500,000) annually, could also benefit from this procedure.

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