

MUSCLE ENZYME CHANGES FOLLOWING A WHIPLASH INJURY

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This study was a prospective evaluation of serial muscle enzyme changes in 25 consecutive patients who were suffering from neck pain following a rear end motor vehicle accident. The objectives were to assess if muscle damage occurs and to quantify it following a whiplash injury.

It is often stated that a whiplash injury is a soft tissue injury consisting of damage to the muscles and ligaments of the neck. However no study has looked at this. MRI scans occasionally show haematoma within the paravertebral muscles but are not sensitive enough to assess muscle damage. Creatinine kinase has been shown to be the most sensitive indicator of muscle damage

Twenty-five consecutive patients suffering from neck pain following a rear end collision were recruited. Serial creatinine kinase measurements were taken on three consecutive days including the day of the accident and a control value at three months following the injury. Only patients with isolated whiplash injuries were included.

There were no significant rises in creatinine kinase in any of the patients in the study, even in two patients who had to be hospitalised because of the severity of their symptoms.

We have found no evidence that the symptoms arising after a whiplash injury are due to muscle damage and other avenues need to be explored.

INITIAL MANAGEMENT OF WHIPLASH INJURIES

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The purpose of the study was to observe the initial management of a cohort of patients attending Accident and Emergency departments within an English Health Authority Region with a diagnosis of whiplash. The aims were to record the demographic and epidemiological data and any differences in the use of initial management modalities in particular the prescription of soft collars or use of radiographic imaging. Whiplash-associated disorders are a modern epidemic in many countries. The current literature indicates the lack of efficacy for the use of soft collars in the condition's initial management.

Data were collected by review of all the casualty records during a 12-week period across seven District General Hospitals. Demographic, epidemiological and initial management data were recorded. Processing was by computer database.

Nine hundred and twenty eight cases were collected. This figure gave an estimate for an annual incidence of 200 per 100 000 per year. 57% of patients were female, 73% were drivers, with 44% involved in a rear impact and 25% a front-end collision. There was a wide variation in the use of soft collars between hospitals from less than 1% of cases in one hospital to 68% of cases in another being prescribed a soft cervical collar on discharge.

The literature on whiplash-associated disorders (W-AD)¹ is colossal. The current consensus supports the lack of efficacy of soft collars in the initial management of whiplash patients. The studies by Mealy et al³, McKinney⁴ and Borchgrevink⁵ et al all indicate their use is detrimental to patient short and medium term outcome. The estimated cost to Society of W-AD is in Europe put at an annual figure of 5-10 Billion Euros and \$29 Billion in the USA⁶. It is expectant of the Medical profession to try and mitigate the patients' loss with the best evidence based initial management of whiplash.

References

1. Scientific Monograph of the Quebec Task Force on Whiplash-Associated disorders: Redefining "whiplash" and its management. *Spine* 1995;20S.
2. Dolinis J. Risk factors for 'whiplash' in drivers: a cohort study of rear-end traffic crashes. *Injury* 1997;28(3):173-9.
3. Mealy K, et al. Early mobilisation of acute whiplash injuries. *BMJ* 1986;292:656-7.
4. McKinney L. Early mobilisation and outcome in acute sprains of the neck. *BMJ* 1989;299:1006-8.
5. Borchgrevink G. Acute treatment of whiplash neck sprain injuries. *Spine* 1998;23:25-31.
6. Schmid, P. Whiplash-associated disorders. *J Suisse Med* 1999;129(38):1368-80.

PATTERNS OF INJURY TO THE CERVICAL SPINE RELATED TO THE DIRECTION AND MAGNITUDE OF IMPACT TO THE HEAD

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The objective of this project was to determine, for fatally injured car and truck occupants, if there were patterns of injury to the cervical spine, which could be related to the direction, and magnitude of the impact to the head. A detailed examination of the cervical spine was carried out in 43 cases. The spine was removed at post mortem examination, frozen and cut into sections, each 2 mm thick, in the sagittal plane. Each section was examined microscopically and the injuries recorded. For each case, the Coroner's records were examined and the events of the crash re-constructed from the available evidence to determine the direction and point of impact on the head, if any, and magnitude of the impact, if possible. Sufficient information was available in 29 cases. Impact velocity ranged from about 10 km/h to 70 km/h. There were 10 impacts to the front of the head, five impacts to the top, 13 impacts to the side of the head (eight left, five right), and one to the rear. The presence or absence of injury was recorded at thirty possible location of injury along the cervical spine between the occipito-cervical joint and the C7-T1 intervertebral disc. Impacts to the top of the head tended to produce more widespread injury, compared with front and lateral impacts, given impacts of similar magnitude. Impacts to the top of the head produced an injury distribution that was symmetrical laterally with a concentration in the lower part of the cervical spine and with a relatively high ratio of bony injury to disc injury. For frontal impacts the injuries to the spine were also symmetrical about the midline, but with a concentration at the upper and lower levels, and in the intervertebral disc structures. For left lateral impacts to the head, injuries appeared symmetrical on both sides of the spine, but there was a concentration of injury in the upper region of the spine more than at the lower. Compared with the frontal and top impacts, there were fewer injuries to the intervertebral discs and the cervical bodies.

HEALTH-STATUS AND BIOMECHANICAL OUTCOMES FOLLOWING ANTERIOR CERVICAL SPINE FUSION (ACF)

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Clinical outcomes following anterior cervical spine fusion (ACF) have generally been defined in relation to surgical criterion such as fusion success, surgical complications and neurological recovery. While these issues are clearly important, the need for a broader evaluation of health status outcomes following spinal fusion surgery is being

increasingly recognised. The aim of this study was to evaluate short-term health-status and biomechanical outcomes following ACF.

Twenty patients with a mean age of 48 years (SD=7) were evaluated before ACF surgery (C5/6 n=14, C6/7 n=6) and at six weeks and six months post-surgery. Lateral cervical spine radiographs, including flexion and extension functional views, were used to measure resting cervical curvature and sagittal mobility. A modified Cobb technique (C2 to C7) was used to measure cervical spine curvature while the segmental range of motion (SROM) at each disc segment was determined from the functional radiographs using a superimposition technique. Patient-reported head, neck and arm pain intensity was measured using visual analogue scales. Neck-related disability was measured using the Northwick-Park Neck Pain questionnaire and a generic quality of life survey (SF-36) was also completed. Standard errors of measurement for repeated measures of SROM and cervical curvature were 1.3° and 1.1°, respectively.

At both post-operative assessments there was no significant change in cervical curvature ($p=0.08$) or total sagittal range of motion (C2/3 to C6/7; $p=0.10$). In the 14 patients who had C5/6 fusion there was no change in the range of motion at any of the unfused segments ($p=0.31$). Head, neck and arm pain intensity scores were all significantly lower at six months ($p<0.03$) as were the Northwick Park disability scores ($p<0.01$). Similarly, the physical and mental health components of the SF-36 quality of life survey were both significantly improved at the six-month follow-up ($p<0.0001$).

While acknowledging the absence of a control group for comparison, the results indicate significant improvements in primary health-status outcomes of pain, disability and quality of life, six months following ACF. This not only quantifies the level of recovery following ACF but also confirms the value of these measurements in providing a broader outcome assessment for this surgical procedure. Changes in sagittal segmental motion following ACF were not identified in this study. On-going evaluation of biomechanical and patient-related outcomes following ACF will assist in determining treatment effectiveness and in developing realistic expectations of post-surgical outcome.

THE EFFECT OF REPEATED INJURY TO LUMBAR NERVE ROOTS IN THE RAT

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This study was designed to examine pain-related behaviours following repeated lumbar nerve root injury in the rat.

To gain a further understanding of the role of central neuroinflammation associated with chronic low back pain and lumbar radiculopathy (LR), this research studied the relationship between pain related behaviours (mechanical allodynia) and nerve root injury in an animal model for repeated injury of the L5 nerve root.

The pathophysiologic mechanisms resulting in chronic low back pain and radiculopathy remain obscure. In clinical practice the onset of chronic low back pain with radiculopathy secondary to intervertebral disc prolapse is often preceded by bouts of pain which are similar in nature but are self-limiting. We hypothesise that the initial injury to the nerve root or dorsal root ganglion produces central neuroimmune changes which “prime” or “sensitise” the spinal cord, with a greater and more prolonged response to subsequent injury. To investigate this hypothesis we developed a model for repeated lumbar nerve root injury in the rat.

Twenty-one male Holtzman rats (weighing 225 – 250 g at the time of the first surgery) were divided into two treatment groups, (1) sham group (n=7) which had a left L5 hemi-laminectomy exposing the left L5 nerve root. (2) chronic group (n=14) which had a left hemi-laminectomy and the left L5 nerve root was ligated loosely with

chromic gut. Following surgery, mechanical allodynia was assessed in both hind paws up to 42 days post-operatively, at which time all animals in the study underwent a second procedure. The sham group had repeated exposure of the L5 nerve root. The chromic group had repeated exposure of the left L5 nerve root and repeated ligation of the nerve root with chromic gut. Following the second procedure, mechanical allodynia were assessed in both hind paws up to 42 days post-operatively.

Allodynia was observed in both ipsilateral and contralateral hind paws following initial surgery in the chromic group. Allodynia was not observed in the sham group. The allodynic response was greatest in the left (ipsilateral) hind paw. Following repeated surgery the repeated injury group had an exaggerated and more prolonged allodynic response compared to the initial injury in both the ipsilateral and contralateral hind paw. The repeated injury sham groups did not exhibit significant allodynia.

Conclusions

An exaggerated and more prolonged allodynic response following repeated injury of the ipsilateral and contralateral nerve root suggest central "sensitisation" following the initial injury. The presence of bilateral allodynia supports a central pathway for modulation of radicular pain following lumbar nerve root injury.

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SCHMORL'S NODES: A POSSIBLE RELATION TO JUVENILE KYPHOSIS

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Schmorl described intravertebral disc herniations in 38% of adults, most often in lower thoracic and upper lumbar vertebrae. He noted the link between Schmorl's nodes and Scheuermann's disease, but the mechanism linking the two has never been adequately elucidated.

In a study of 110 autopsy lumbar spines, which included the thoracolumbar junction, specimens including the middle third of the disc and adjoining vertebral end plates were taken from 20 specimens in the age range five years to 35 years. This included specimens from 10 children, five adolescents and five adults. A search was made for cartilage plate fractures or nodes in the children but all the adolescents and adults showed probable Schmorl's nodes. These specimens already formalin fixed, were dehydrated, embedded in low viscosity nitrocellulose and sagittally sectioned at 100 μm thickness to be stained with haematoxylin and light green and mounted for histological examination. In addition, the number of cases showing Schmorl's nodes out of 110 sagittally sectioned spines from individuals in the age range five to 97 years was counted; a similar count was made in 80 normal thoraco-lumbar spine films from patients in the age range nine to 33 years. The prevalence of Schmorl's nodes was found to be similar to Schmorl's account, lower in radiographs than in autopsy specimens, with no nodes in young children, a low prevalence for nodes in older children and a higher but similar prevalence in adolescents compared to adults.

Histological examination of the 20 selected specimens showed no nodes or cartilage plate fractures in children, but confirmed the presence of multiple nodes in the five adolescents and five adults, the youngest specimen with nodes being aged 13 years. The nodes all showed fracture of the cartilage plates with herniation of nuclear material into the spongiosa. In two cases, aged 13 and 17 years, part of the herniating material bore a resemblance to notochordal tissue, normally found only in infants and young children. In one case, a 16-year old male, the herniated material,

at T12-L1, in addition to entering the vertebral spongiosa, had spread horizontally between the cartilage plate and the bony end plate. There was no obvious vertebral deformity. Adolescent and young adult specimens showed a marked increase in vascularity of the cartilage plate and bone around the herniations, compared to the end plate of controls with no nodes.

It is not known how frequently Schmorl's nodes spread laterally to separate the cartilage growth plate from the metaphysis but one would expect a disturbance of growth in any such instances. The increased vascularity around nodes may weaken the vertebral end plate and favour such lateral spread of nuclear material. Increased vascularity in the region of nodes may also favour the survival of notochordal tissue, which would normally die within the first decade of life.

Reference

Schmorl G, Junghanns H. The Human Spine In Health and Disease. 2nd American edition. Grune and Stratton, New York, 1971.

THORACOLUMBAR SPINAL DEFORMITIES IN THE SAGITTAL PLANE

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Kyphosis is a progressive spinal disorder that can affect children or adults. This disorder can be in the form of hyperkyphosis or sharp angular gibbus deformity. Some of the common aetiologies of kyphosis include postural round-back, Scheuermann's disease, congenital kyphosis, neuromuscular disorders, trauma, tumours, infection, iatrogenic flat-back syndrome, and arthritis. Indications for surgery include progressive deformity or unrelenting pain despite nonoperative treatment, neurological symptoms, and functional disability associated with the deformity.

Kyphosis surgery can be long, difficult cases with potentially great rewards for the patient. A variety of treatment methods can be used with proper patient selection. This study reviews the presentation and aetiology of a series of kyphosis cases treated by a single surgeon and critically evaluates the various methods used surgically.

Fifty-nine consecutive cases of kyphosis surgery were identified from a prospectively collected database. All hospital and office charts were reviewed and clinical follow-up obtained.

Follow-up was two years or greater. Twenty-six of the patients underwent simultaneous surgical approaches, seven staged surgeries on the same day and five on separate days, four anterior only and 17 posterior only. There were 31 females and 28 males, with an average age of 45 years (range 8 - 87). There were three cases of Scheuermann's kyphosis, 17 of post-traumatic kyphosis, two of post-laminectomy, seven of neuromuscular kyphosis, six of kyphosis associated with tumour, eight of kyphosis associated with infection, six of kyphoscoliosis, six of flatback syndrome, one ankylosing spondylitis and three of congenital kyphosis. Operative times were somewhat lower for simultaneous versus same day staged surgeries. Total blood losses were higher for separate day staged, but operative times were less than same day or simultaneous. Overall blood loss was 1400 ml (range 200 - 5000 ml) and the average number of units transfused was four. Six cases of instrumentation problems required further surgery. There were two infections and 14 patients complained of back pain on follow-up.

In properly selected cases, anterior, posterior and combined approaches all can be safely used to treat kyphotic deformities. Posterior pedicle subtraction osteotomy was utilised for correction of kyphosis associated with ankylosing spondylitis and flat-back syndrome. Simultaneous approaches may be used in many cases to decrease blood loss and operative time.

DECISION ANALYSIS AND SPINAL FUSION FOR LOW BACK PAIN.

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Despite agreement about the success rate of spinal fusion for back pain of about 70% most authorities disagree about the reasonableness of the procedure, presumably because of differences of opinion regarding the value of the clinical outcomes of success or failure. Decision analysis is a technique that analyses decision making under conditions of uncertainty. The consequences of a decision to operate or not on a patient has four possible outcomes - successful surgery, unsuccessful surgery, successful avoidance of surgery (spontaneous recovery) and unsuccessful avoidance of surgery (continuation of chronic pain). Patients can be asked to attach a value (utility) to each of these outcomes by the use of a visual analog scale with the end points being the most desirable and the least desirable outcome respectively. If the probability of each of the four outcomes is multiplied by its utility and the result summed for the outcomes associated with each decision, an expected value for each decision can be obtained. Decision analysis states that the decision with the highest expected outcome is the preferable one.

Thirty cases with chronic low back pain were subjected to a formal clinical interview to determine the utility of outcome for successful and failed outcomes of a hypothetical anterior and posterior fusion. Utility values were also obtained for the outcomes of spontaneous recovery and of continued chronic pain. The procedure was repeated with a hypothetical procedure of a laparoscopic anterior fusion. Sensitivity analysis was conducted using this data and a presumed spontaneous recovery probability of 0.1 to calculate a breakeven probability for successful surgery. This probability represents the probability for successful surgery at which a patient could not choose between the options of surgery or no surgery.

The mean breakeven probability for successful open surgery was 0.26 (SD 0.33) and 0.08 (SD 0.38) for successful laparoscopic surgery. Data were available for duration of symptoms, visual analog pain scale (VAS), North American Spine Society (NASS) back pain and neurogenic symptom scores and the short form (SF) 36 mental health subscale. Stepwise multiple regression analysis suggested that the NASS low back pain disability score was the most important regression variable ($p = 0.0017$ for open surgery and $p = 0.0001$ for laparoscopic surgery). A small extra effect was contributed by the VAS ($p = 0.06$ for open and $p = 0.02$ for laparoscopic surgery). For open surgery the regression formula is: Breakeven probability = $0.69 - 0.24 \times \text{NASS} + 0.06 \times \text{VAS}$. For laparoscopic surgery the formula is: Breakeven probability = $0.69 - 0.33 \times \text{NASS} + 0.07 \times \text{VAS}$. The model explains 31% of the variance for open surgery and 43% of the variance for laparoscopic surgery.

Most patients with chronic low back pain are prepared to accept success rates for surgery that are substantially lower than the average quoted success rates in many series, indicating that most of these patients see fusion surgery as a reasonable option. Patients are more likely to accept lower rates of success if they have higher back pain disability scores and if the surgery is perceived as less invasive.

THE VBR SPINAL RECONSTRUCTION SYSTEM

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The need for a vertebral body replacement for tumour has been established¹ and its use for fracture fixation validated. There are many products on the market; however the experience of the senior authors led to the concept that there was a need for an anatomical design with more flexibility and security of implantation while also

addressing the tribiology and imaging requirements of a Vertebral Body Replacement (VBR).

The designers original anatomical studies², using measurement and modelling of specimens, showed that the size and shape of the thoracic and lumbar vertebral bodies are predictable and follow a simple formula. This produced a 'common curve' with an exponential line *x against 1/y*.

The design incorporated these findings with an additional unique and important feature of a recessed posterior wall to minimise the risk of canal intrusion and the resultant kidney-shaped cross section gives added resistance to compressive loads. The VBR has end-caps, which allow implantation flexibility with their plain or lordotic contours and added strength and security with their flat or pinned end-caps.

To date several European centres have experience of the VBRs use. A few cases are shown to illustrate its clinical applications: burst fracture L1- thoracolumbar plasmacytoma.

The VBR spinal reconstruction system was based on the concepts for a simple design allowing ease of use, reproducible results across a range of applications for the thoracic and lumbar spine. The designers feel that the VBR spinal reconstruction system offers a spinal surgeon security and flexibility having addressed the end-user requirements during its conception, design and manufacture.

References

1. Enkaoua et al. *Spine* 1994;19:2774-9.
2. Harrison DJ, Lehovskiy J. New thoughts on vertebral morphology, Proceedings of the British Scoliosis Society.

POSTERO-LATERAL LUMBAR FUSION USING OP-1: A MODEL USING PATIENTS WITH DEGENERATIVE SPONDYLOLISTHESIS – PRELIMINARY RESULTS

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There is no published prospective controlled trial of the use of OP-1 alone in postero-lateral spinal fusion in humans. The assessment of spinal fusion is made more difficult when metallic implants are used and the usual criteria for randomisation require large numbers of patients. Patients with neurogenic claudication due to lumbar spinal stenosis with associated degenerative spondylolisthesis are best treated, when surgery is required, with decompression laminectomy and in situ postero-lateral fusion. The addition of internal fixation has not been proven to produce superior clinical results. They therefore provide a group of patients in whom the development of a postero-lateral spinal fusion can be more easily assessed radiologically.

A pilot study of patients aged from 45-80 who were to undergo decompression laminectomy and postero-lateral fusion in the lumbar spine had a fusion undertaken with autograft taken from their iliac crest on one side and OP-1 in Carboxymethylcellulose (CMC) "putty" on the opposite side. Approximately 12.5 g of autogenous bone was used on one side and a standard quantity of OP-1 and collagen matrix in the CMC putty on the other side. Clinical, questionnaire and radiological assessment with plain x-rays to be undertaken at six weeks, three, six, nine and 12 months post-operatively. A CT scan to assess the volume of fusion and incorporation of the bone graft is to be undertaken at 12 months.

As of the end of February 2000 there were five patients who had been enrolled in the trial. The maximum follow up is 12 months and the least is three months. All patients thus far show development of bone on both the autograft and the OP-1 sites. Clinical progress has been excellent. The 12-months follow up investigation with x-rays and CT scan to assess the volume allows a more objective assessment of the success of the fusion as well as the volume of bone produced.

A model using patients undergoing lumbar spinal decompression laminectomy and postero-lateral fusion allows patients to be used as their own control. Radiologic progression of the bone formation has been excellent thus far.

CYLINDRICAL THREADED CAGES FOR LUMBAR DEGENERATIVE DISC DISEASE A PROSPECTIVE LONG TERM RADIOLOGICAL STUDY

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Cylindrical threaded cages have been used with increasing frequency over the last ten years for the treatment of degenerative disc disease. After initial favourable reports, concerns have been raised recently with regard to the long-term stability of the implants, potential for bone ingrowth, loosening and need for re-operation. This study is a prospective radiological analysis of 68 patients undergoing primary lumbar interbody stabilisation using cylindrical titanium threaded cages with a minimum follow up of two years.

Sixty-eight patients who underwent lumbar interbody stabilisation using cylindrical titanium threaded cages with a total of 90 operated spinal motion segments (L3-4: 11; L4-5: 38; L5-S1: 41) were analysed prospectively with a minimum follow-up of 24 months, average 44.6 months. All patients underwent plain radiographs and CT scans prior to the surgery with radiological imaging at six months, twelve months and at the time of the last follow up. Age ranged from 28 to 64 with an average of 44. Imaging analysis included anterior and posterior disc height ratio, prosthesis migration, lordosis/kyphosis angle, lucent zones around the prosthesis, bony bridging and intervertebral angle.

All imaging was assessed independently by the principal author who had not been involved in the treatment of the patient and an experienced musculoskeletal radiologist.

Of the 68 patients, 29 underwent interbody stabilisation with cages only (Group 1), 15 had interbody cages supplemented with in situ posterolateral bone graft (Group 2) and the remaining 24 had interbody cages supplemented by posterolateral pedicle screw fixation.

In Group 1, five of 29 patients (17%) exhibited radiological evidence of loosening at last follow up. Prosthesis migration was seen in three cases (9%) with one patient requiring re-operation. In Group 2, two of 15 patients exhibited radiological loosening and prosthesis migration (13.3%) with one requiring re-operation. In Group 3, two patients (8.3%) had positive lucent zones but no prosthesis migration and no further surgery. Intervertebral disc space height was increased in all patients post-operatively with gradual loss of correction in Group 1 and 2 of approximately 50% at follow up and no significant loss of correction in Group 3. One case of late infection was recorded in Group 2. No loosening and/or prosthesis migration was seen at L5-S1 with four of nine cases of radiological loosening at L3-4 and the remaining five at L4-5.

Cylindrical threaded cages in combination with posterolateral bone graft allow satisfactory bony ingrowth and long term radiological stability. Risk factors for loosening, prosthesis migration and non-union are represented by the use of cages alone, L3-4 and L4-5 levels, early post-operative loss of disc height, osteoporosis and infection. It is recommended that supplementary pedicle screw fixation be used when cylindrical cages are employed at L3-4 and L4-5.

ANTERIOR CERVICAL INTERBODY FUSION WITH A NEW TITANIUM CAGE - A PROSPECTIVE MULTICENTER STUDY IN 138 PATIENTS

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A new implant for cervical interbody fusion has been developed, which combines characteristics of the Cloward and the Smith-Robinson techniques. It is a dome-and-wing shaped Titanium cage, which - in analogy to the Cloward technique - is fixed by a central interbody burrhole providing an additional area of contact to the vertebral spongy bone for fusion. The loadbearing rectangular lateral wings of the implant fit into the disc space. They are slightly wedge-shaped to support the lordotic position of the cervical spine. The implantation technique has no difficulties and can be easily incorporated into the standard surgical technique for anterior interbody fusion. The clinical and radiological results in 138 patients have been evaluated.

Out of June 1999, 138 patients (mean age 49.45 years, 78 female, 59 male) with mono- or multisegmental degenerative spine disease with signs of nerve-root and/or myelon compression have been treated microsurgically. Anterior discectomy, decompression of the myelon and nerve-roots and subsequent interbody fusion have been performed. 156 levels (single level, 112; two levels, 19; three levels, 2) have been operated. In 27 segments the cages were filled with autologous bone, in 129 segments with bone substitute (β -tricalcium-phosphate). Radiologically 39 patients had a sequestered disc herniation, 110 had signs of radicular involvement and 23 patients suffered from cervical myelopathy. Clinical and radiological follow-up examinations were performed at the time of discharge from hospital, six weeks, three months and six months postoperatively.

The clinical follow-up showed an excellent or good result with significant reduction of radicular pain or - if present - radicular deficits in over 93% of all patients. Insufficient pain relief and/or unchanged neurological deficits were found in seven (6%) patients. Worsening of the neurological signs occurred in one (1%) patient. The PROLO socio-economic function score increased from preoperative 6.59 points to 8.83 points after six months. In five (4%) patients subsidence with loss of correction or persisting nerve-root compression was observed, three (2.5%) of them requiring surgical correction.

The new titanium cage was easy to handle and provided immediate stability in all cases. It allowed - if necessary - segmental distraction and restoration of the sagittal profile of the cervical spine. The clinical outcome was good or excellent in more than 93% of patients, including those with myelopathic signs. There was no substantial implant migration or dislocation. There were no implant-related complications. Until today no insufficient fusion or pseudarthrosis have been observed. Follow-up will be continued.

INTERVERTEBRAL DISC DEGENERATION AND REGENERATION

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In recent years, there have been significant advances in the diagnosis and treatment of lumbar intervertebral disc disease. In managing patients with discogenic low back pain, one must make the correct diagnosis by ruling out non-mechanical aetiologies and considering appropriate imaging studies such as MRI and discography. Nonoperative therapy is the mainstay of treatment, especially self-motivated

conditioning and back exercise program. Lumbar fusion is considered as an option in those patients with unrelenting pain and disability despite conservative treatment for at least six months. Fusion methods are evolving, particularly with the use of minimally invasive techniques such as cages. Intradiscal electrothermal therapy (IDET) is a new technique to alter biomechanics and nociceptors in the annulus fibrosus. While preliminary results are encouraging, long-term controlled results should be considered to better assess the merit of these procedures. In choosing either lumbar fusion or IDET, proper patient selection is the key to the successful outcome. Further research in biomechanics and biology of the intervertebral disc is needed to help diagnose degenerative disc disease and treat with minimally invasive techniques. Reported here are studies on the biomechanical relationship between intervertebral disc degeneration and kinematic characteristics of the lumbar motion segment, and intervertebral disc regeneration using bone morphogenetic protein –7 (OP-1).

Biomechanical Study

A total of 106 motion segments (T1-L1 to L5-S1) were obtained from 44 cadaveric lumbar spines (18 female and 25 male) with a mean age of 69 years. Following the MR scan the motion segment underwent nondestructive flexibility tests using pure moments of flexion-extension (FE), lateral bending (LB) and axial rotation (AR) applied in six load steps of 0.5, 1.6, 3.6, 4.7, and 6.6 Nm. Resultant rotational movements were measured using a 3-dimensional motion analysis system. Degenerative changes in the disc and facet joints were graded separately by two experienced spine surgeons. Disc degeneration (DD) was graded from I (normal) to grade V (advanced) according to Thompson's criteria using T-2 weighted sagittal images and facet degenerative changes from I (normal) to grade IV (advanced) by Grogan et al. Facet degeneration was assessed by cartilage degeneration (CD), subchondral sclerosis (SS), and osteophyte formation (OS). DD was found to have a significant positive linear correlation with CD ($p < 0.01$) while it has no correlation with SS and OS. In FE and AR the motion increased with the progression of DD up to grade IV and decreased when DD reached grade V. In LB the greatest motion was observed in DD grade III. Significant ROM difference was noted between grade II and grade IV in FE and AR ($p < 0.05$). The effect of CD on the motion was similar to that of DD. The segment with higher CD grade showed significantly larger AR ($p < 0.05$). The effect of SS on the motion was significant ($p < 0.05$) but opposite to that of DD and CD. The segments with higher SS grades had significantly less ROM in all directions, and the effect of OS on the motion, however, was found to be not significant.

OP-1 Study: Recombinant Osteogenic Protein-1 upregulates extracellular matrix metabolism by rabbit annulus fibrosus and nucleus pulposus cells.

This study was performed to determine if rhOP-1 also is effective in promoting matrix synthesis and matrix formation by NP and AF cells cultured in alginate beads. Cell Culture: Annulus fibrosus (AF) and nucleus pulposus (NP) from New Zealand white rabbit lumbar intervertebral discs (IVD) were separately dissected, and cells were released from each tissue by sequential enzyme digestion, encapsulated in 1.2% low-viscosity alginate, and maintained in DMEM/F12+10% FBS with a daily change of media. The MTT analyses (cell proliferation and DNA content) revealed that rhOP-1 had a significant mitogenic effect at high concentrations only (AF: 100 and 200 ng/ml, $P < 0.01$; NP: 100 ng/ml, $P < 0.01$). Proteoglycan (PG) Synthesis: rhOP-1-treatment resulted in a significant dose-dependent increase in PG synthesis by both the AF and NP cultures maintained in the presence of 10% FBS (rate of synthesis as % of control: AF = 230%; NP = 460%). Collagen Synthesis: rhOP-1 stimulated collagen synthesis by both NP cells and AF cells in a dose-dependent manner. The results presented here provide evidence of the ability of rhOP-1 to stimulate the metabolism of both AF and NP cells.

Effects of recombinant human OP-1 (rhOP-1) injected within a lumbar IVD in the rabbit on the metabolism of the IVD and its resident cells.

Eighteen New Zealand white rabbits weighing 3-4 kg were induced with general anesthesia, and X-rays of the lumbar spine in lateral view were first taken to obtain pre-injection baseline values for disc heights. Lumbar discs (L2-L5) were then exposed through a posterolateral retroperitoneal approach, and rhOP-1 (2 µg in 10 µl of saline) was injected into the centre of the nucleus of three consecutive IVD (L2/3, L3/4, and L4/5). In the case of the control group, 10 µl of saline was injected in the same way. Two, four and eight weeks after the injection, X-rays of the lumbar spine were again taken under general anaesthesia and three rabbits of each group were euthanased at each time point. X-ray films obtained before operation and at euthanasia were digitised and the IVD body's height and disc height were measured by NIH-image software. IVD height was expressed as disc height index (DHI) using the method of Liu et al with a slight modification ($DHI = \text{IVD height} / \text{adjacent IVD body height}$). The NP was bluntly separated in each case from the AF. All specimens were digested with papain and were analysed for contents of (i) DNA by the Hoechst 33258 dye and fluorometry, (ii) PG by the DMMB dye assay and (iii) hydroxyproline as a measure of collagen by reverse-phase HPLC and PICO tag labeling after acid hydrolysis. Two weeks after the injection, the mean % DHI of injected discs in the OP-1 group was significantly higher than in the saline group. It remained higher than in the saline group at the four and eight weeks time points but the difference did not reach statistical value, possibly because of the small number of animals studied. In the saline group, but not in the OP-1 group, the PG content of the NP in the injected discs was lower than in the non injected adjacent control disc at all time points. The PG content in the OP-1 group was significantly higher than in the saline group at the two weeks time point. OP-1 was effective in promoting *in vitro* the repair of the extracellular matrix around NP and AF cells, and intradiscal administration of OP-1 *in vivo* results in significant increases in disc height and PG content of NP. These *in vivo* and *in vitro* findings illustrate the potential of OP-1 to promote NP regeneration in humans.

Discussion

Intervertebral disc disease is ubiquitous and it is a challenge to identify symptomatic disc degeneration and treat it with predictable successful outcomes. Further research in the fields of biomechanics and biology related to the intervertebral disc will help achieve these goals.

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SHOULD SPINE SURGERY BE A SEPARATE INDEPENDENT SURGICAL SPECIALTY? THE ACCREDITATION OF SPINE SURGERY TRAINING - A POINT OF VIEW

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This is not a scientific paper, but a point of view regarding this controversial topic that is receiving careful attention throughout the world.

First: Should spine surgery be a separate and independent surgical specialty? The American Board of Medical Specialties' criteria for the establishment of a new specialty include (1) a separate and distinct organ system; (2) significant increase and development in the knowledge and techniques related to the organ system; and (3) the specialty is not already adequately covered by an existing specialty. Surely the spine is just as distinct and separate an organ system as the cardiovascular

system or the urological system. There certainly have been major increases and developments in the knowledge and techniques of spine surgery over the past thirty years. The author believes there is general agreement that spine surgery should be a separate and independent surgical specialty.

Second: The accreditation of spine surgery training: There is no such consensus on this issue. Spine surgery (like hand surgery) is not the purview of just one surgical specialty. Spine surgery is a special case, as it has developed by, and still receives, major contributions from both neurosurgery and orthopaedic surgery. Thus it cannot be controlled by one or the other; it requires a joint venture and equal participation and control from each. The path taken by U.S. hand surgeons should not be followed. Certificates of Added Qualifications (CAQS) given by one discipline will not be accepted by the other. Therefore, organised neurosurgery or orthopaedic surgery cannot solve the problem. Neither can the specialty spine societies because they either are too focused and do not consider spine surgery in its entirety (e.g., The Scoliosis Research Society), or they are multidisciplinary (e.g., North American Spine Society). The accreditation of spine surgery and the certification of spine surgeons must be by spine surgeons, for spine surgeons - just as with other medical specialties. Therefore, after careful consideration, the American Board of Spine Surgery was incorporated in 1997, knowing that whilst it had to be independent of organised neurosurgery and orthopaedic surgery, it had to proceed against their opposition to eventual accreditation and acceptance by the American Board of Medical Specialties. This point of view paper will outline the progress so far, discuss the advantages and disadvantages of spine specialisation, and what the future holds in this long political journey.

References

1. Crockard H.A. Training Spinal Surgeons. *J Bone Joint Surg* 1992;74-B;74.
2. DeWald, R.L. The Textbook of Spine Surgery, Y-XV 2nd edition. Lippincott-Raven, 1997.
3. Kostuik J.P. Training Spinal Surgeons. *J Bone Joint Surg* 1992;74-B;786.
4. Margulies JY. Revision Spine Surgery, XV, Mosby, 1998.

A CONTROLLED TRIAL OF INTRADISCAL ELECTROTHERMAL ANULOPLASTY FOR INTERNAL DISC DISRUPTION

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Intradiscal electrothermal anuloplasty (IDTA) has been popularised in the United States as a treatment for painful internal disc disruption (IDD), but on the basis of uncontrolled audits. To test the efficacy of this procedure we undertook a controlled trial.

Of 110 patients presenting with low back pain, 53 satisfied the diagnostic criteria for IDD, prescribed by the International Association for the Study of Pain. Of these patients, 36 consented to undergo IDTA. The remaining 17 patients were denied permission by their insurance companies to undergo IDTA, and constituted a control group. The control therapy consisted of an established physical therapy rehabilitation program. Baseline measures were obtained from all patients with respect to visual analog pain score, Oswestry disability score, drug consumption, and return to work. The same instruments were administered to all patients at three, six and twelve months after treatment.

At three months, only one control patient obtained any significant degree of relief of pain, compared to 23 in the index group. In the operated group, relief of pain was sustained at six months, and at 12 months; and was associated with improvement in disability, reduced drug-use, and a return to work rate of 53%. Relief of pain by 50% or more to a level of less than five on a 10-point scale strongly predicted return to work. Depending on the stringency of criteria used, the success-rate of IDET may be

as low as 37% or as high as 62%, with confidence intervals of $\pm 16\%$. Within this range, however, 19% of patients obtained complete relief of their pain at 12 months.

In patients with a rigorously established diagnosis, IDTA seems to be an effective therapy for IDD. No other treatment for IDD has been shown to achieve complete relief of pain, sustained at 12 months. Improvements in technique are expected to improve success rates.

A MATHEMATICAL MODEL FOR PREDICTION OF SPINAL KINEMATICS AND INJURY

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Motor vehicle accidents frequently cause injuries to the spine resulting in long term disability. The mechanisms of injury however, remain poorly understood. Many of the currently available crash test dummies (EuroSid and Hybrid III) are deficient in consideration of the spine, lacking the correct biofidelic behaviour to accurately predict injury. We have developed a detailed mathematical model of the whole spine for the investigation of spinal kinematics and injury sustained during passenger vehicle impacts.

The model uses finite element analysis, which allows for the high level of geometric detail necessary to capture complex stress distributions within each vertebra. Surface geometry was reconstructed using digitised co-ordinates taken from six vertebrae (T10 to L3). The location, geometry and physical properties of six ligaments (anterior, longitudinal, posterior longitudinal, ligamentum flavum, interspinous, supraspinous and capsular) and the intervening intervertebral discs were then added. The model was extrapolated to represent the whole thoraco-lumbar spine (T1-L5). An independently developed model of the cervical spine (with muscle and ligaments representations) was then added to the thoraco-lumbar model. The LS-DYNA (Livermore Software Ltd) finite element analysis code was used for simulation of a wide range of non-linear dynamic scenarios including viscoelastic behaviour. Simplifications of the model included replacement of deformable material with rigid materials, replacement of complex joint with non-linear springs, and substitution of detailed ligament representations with springs and dampers. The complete spine model was then embedded into a dummy model to generate a realistic 'crash loading scenario' for the spine.

The model produced has been validated against published data on stiffness, strength, range of motion and known physical properties of individual functional spinal units 1-3. Further validation has been provided by both volunteer and cadaveric testing. Loads representing a typical frontal impact were then applied to the model. Analysis showed deflections typically seen in passenger vehicle impacts. Ligamentous injury was predicted by monitoring forces and deflections within the model. The model predicts bone stresses at which compressive wedge fractures, fractures of the pedicle and neural arch are known to occur.

A finite element model comprising some 30 000 elements has been developed for analysis of spinal injury. The model has been validated against known material properties and data obtained from both cadaveric and volunteer testing. The model accurately predicts ligamentous and bony failure. We hope the model will provide the basis for the development of casualty reducing design strategies within the automotive industry.

References

1. White AW, Panjabi MM. *Clinical Biomechanics of the Spine* 2nd ed. JB Lippincott 1990
2. Osvalder AL, Neumann P, Ldvsund P, Nordwell AJ. *Biomech* 1990;5:453-460.
3. Myklebust JB, Pintar F, Yoganandan N, Cusick JF et al. *Spine* 1988;13:5526-31.

DISC DEGENERATION

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The hypothesis that compressive forces applied to the intervertebral disc over a long period of time cause disc degeneration was tested in vivo in a dog model.

Coil springs were stretched and attached to produce a compressive force (range: 92 to 156 N) across the lumbar intervertebral discs (L3/L4) of twelve dogs. After up to a year, the dogs were killed and their lumbar spines were removed and radiographed. The L3/L4 disc and two controls (T13/L1 and L4/L5) were examined for visible signs of degeneration. Disc composition was assessed by immunohistochemical analysis and enzyme linked immunosorbent assay, and disc chondrocytes were assayed for apoptosis.

No obvious signs of degeneration in the disc (L3/L4) that had been under compression for up to a year could be observed. There was no evidence of disc bulging, annular fissures, or of disc space narrowing. Changes were seen at the microscopic level, although no thickening of the endplate was apparent. The ELISA analysis provided significant data for all three regions of the disc (nucleus, inner annulus, and outer annulus). When comparing the compressed disc with either of the control disc; (1) the nucleus contained less proteoglycans, and more collagen I and II in the compressed disc; (2) the inner annulus contained less proteoglycans and collagen I in the compressed disc; and (3) the outer annulus contained more proteoglycans and less collagen I in the compressed disc. The collagen II differences for the inner and outer annulus were not significant.

Compressive forces applied to the lumbar intervertebral discs of dogs for up to a year do not produce degeneration in any visible form. However, they do produce microscopic changes and numeric changes in the amounts of proteoglycan and collagen in the nucleus, inner annulus, and outer annulus. Our results add no credence to the commonly held belief that compressive forces applied to the intervertebral disc over a long period of time cause disc degeneration. It could be that one-year is too short a time for disc degeneration (in the dog) to manifest in a visible form.

LUMBAR DISC HERNIATION AND SCIATICA: BASIC SCIENCE RESEARCH AND CLINICAL REALITY

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Disc herniation in the lumbar spine can cause nerve root compression and irritation, leading to sciatica. Experimental research has demonstrated that mechanical spinal nerve root compression can cause nerve root ischaemia, oedema, nerve fibre injury etc., all leading to functional changes. During the last 50 years, data have also been presented which indicate that components of nucleus pulposus, such as TNF-alpha, can cause both structural and functional changes in nerve roots without mechanical compression.

Compression of a normal nerve root usually does not cause pain but if inflammation/irritation of the root is present, even minor mechanical deformation can cause radiating sciatic pain. It should also be noted that neurochemical changes may take place in the spinal cord as a result of nerve root injury, indicating the complexity of these issues and the involvement of the central nervous system in sciatic pain physiology. Clinically it is important to recognise that "silent disc herniations" have been demonstrated in at least 20-30% of all adults with MRI. Clinical research has also demonstrated that SLR is generally much more restricted in patients with lumbar disc herniation than in patients with lateral spinal stenosis.

Such observations support the experimental research data that the presence of nucleus pulposus near the nerve root can cause a painful inflammation of the root.

References

Boden SD, Davis DO, Dina TS et al. Abnormal magnetic resonance scans of the lumbar spine in asymptomatic subjects: A prospective investigation. *J Bone Joint Surg* 1990;72A:403-8.

Garfin SR, Rydevik BL, Brown RA. Compressive neuropathy of spinal nerve roots - A mechanical or biological problem? *Spine* 1991;16:162-6.

Jönsson B, Strömqvist B. Symptoms and signs in degeneration of the lumbar spine. A prospective consecutive study of 300 patients. *J Bone Joint Surg* 1993;75-B:381-4.

Olmarker K, Rydevik B, Nordborg C. Autologous nucleus pulposus induces neurophysiologic and histologic changes in porcine cauda equina nerve roots. *Spine* 1993;18:1425-32.

Olmarker K, Larsson K. Tumor necrosis factor alpha and nucleus-pulposus-induced nerve root injury. *Spine* 1998;23:2538-44.

THE INTERRELATIONSHIP OF STRUCTURAL CHANGES IN ADULT DEGENERATIVE SCOLIOSIS AND THEIR RELATIONSHIP TO THE CLINICAL PRESENTATION

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Adult degenerative scoliosis (ADS) has been reported in up to 30% of patients over the age of 50 years¹. ADS may arise as a result of degeneration in a pre-existing idiopathic deformity or de-novo. Unlike their adolescent counterpart who presents primarily with an asymptomatic deformity with the potential to cause problems later in life, the patient with ADS presents primarily with a symptomatic deformity interfering with independence and quality of life.

The development of spinal implants and improved anaesthesia permit effective surgical treatment of patients with ADS. This study reviews the structural changes which contribute to ADS and determines how these changes may affect clinical presentation. The case notes and radiographs of 22 patients over the age of 50 years who underwent surgery for ADS were reviewed. Quantitative analysis of the pre-operative radiographs of the lumbo-sacral spine included measurement of scoliosis, lordosis (L1-S1), and magnitude of the lateral subluxation in the frontal plane. Clinical presentation was assessed in terms of pain pattern (anterior thigh and posterior leg pain), claudication, and abnormal neurological signs. The data were analysed using Spearman's and Pearson's methods to evaluate correlation.

The number and magnitude of lateral subluxations correlated positively with the degree of scoliosis and lordosis, although lateral subluxation at L2-3 may contribute to a thoraco-lumbar junctional kyphosis. Scoliosis and lordosis correlated positively. Spondylolisthesis did not correlate with any other radiological parameter.

Clinical presentation did not correlate with the degree of scoliosis or the presence of spondylolisthesis. Upper lumbar (L2-3, L3-4) lateral subluxation was more likely to present with anterior thigh pain and lower lumbar (L4-5) with "sciatic" type pain. Lordosis was negatively related to pain pattern, claudication, and neurological deficit. The presence and magnitude of lateral subluxation correlated inversely (negatively) with the presence of neurological signs. Claudication did not correlate with any of the structural parameters contributing to the lumbar deformity.

The magnitude of scoliosis and lordosis is dependent on the number of levels and magnitude of lateral rotatory subluxation. The degenerative change in the disc which allow these displacements is the major contributing factor to the severity of the deformity. Although hypolordosis is a frequent finding in ADS, it was more prevalent in smaller curves.

Clinical presentation did not relate to the magnitude or laterality of the scoliosis. Hypolordosis appeared to protect against claudication and neurological deficit. Upper lumbar subluxations were more likely to present with anterior thigh pain and lower lumbar subluxations as “sciatic” pain distribution. Subluxations do not relate to claudication and appear to have a protective effect on development of neurological deficit, making it unlikely that pedicle kinking due to subluxation is a causation of neurological compromise.

Reference

Robin GC. et al. *Spine* 1982;7:355-9.

BIOMECHANICAL STUDIES OF THE DISCO-VERTEBRAL JOINT AND THE RELATIONSHIP TO CIRCUMFERENTIAL DISC TEARS IN THE SHEEP: PRELIMINARY RESULTS

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The integrity of the annulus fibrosus of the intervertebral disc is critically important for normal disc function. There is abundant evidence that the annulus begins to show signs of failure commencing early in life^{1,2}. Failure of inter-lamella bonding in the disc annulus may have major significance for subsequent disc degeneration and the genesis of back pain. The specific aim of this study was to examine the intervertebral disc joint biomechanics of a sheep model with concentric tears.

Twelve adult merino wethers were randomly allocated into two groups with concentric tears introduced by injection with saline (group 1) or needle stick only with no saline (group 2). Each injection was performed in two randomly selected lumbar discs following exposure of the spine under general anaesthetic. Each group was further randomly assigned to be sacrificed at 0, one or three months in preparation for biomechanical testing. A separate non-operated control group was included at time 0 to provide baseline control data (group 0). Biomechanical tests on each intact functional spinal unit (FSU) were performed in left/right torsion, axial compression, flexion, extension and left/right lateral bending. After testing each intact FSU, the tests were repeated on the isolated intervertebral disc³.

A univariate ANOVA with a factorial structure of procedure (group 0, 1, 2), time (0, one, three months) and joint (intact, disc alone) was performed. Significant effects were discovered due to joint for torsion and extension ($P < 0.001$). The effect of procedure alone was also significant for torsion, extension and left bending ($P < 0.001$). Multiple comparisons for procedure showed that for these modes of tests, both group 1 and 2 were significantly stiffer than group 0 ($P = 0.001$) but no different to each other.

The results indicate that the effect of procedure and joint were significant in certain modes of testing. Early degenerative changes do appear to affect the biomechanics up to three months compared to a normal control group. This study is continuing with additional time points of six, 12 and 18 months being available for testing in the near future. It is expected that stronger evidence of biomechanical changes will become apparent after these longer follow up periods have been assessed.

References

1. Hilton RC, Ball, J. Vertebral rim lesions in the dorsolumbar spine. *Ann. Rheum. Dis* 1984;43:302-7.
2. Osti OL, Vernon-Roberts B, Moore R, Fraser RD. Annular tears and disc degeneration in the lumbar spine. A post-mortem study of 135 discs. *J. Bone Joint Surg* 1992;74[B]:678-82.

- Latham JM, Percy MJ, Costi JJ, Moore R, Fraser R D, Vernon-Roberts B. Mechanical consequences of annular tears and subsequent intervertebral disc degeneration. *Clin. Biomech* 1994;9:211-9.

BONE GRAFT SUBSTITUTES

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The gold standard graft material for spine fusion remains autogenous iliac crest bone. Autograft has limited supply, is associated with harvest morbidity, and often results in nonunion. The purpose of this paper is to review the presently available and bone graft substitutes and update knowledge on future bone graft substitutes.

We first developed and validated a rabbit model of posterolateral intertransverse process lumbar spine fusion. We then studied the biology of normal and impaired fusion healing states. Next, we evaluated a variety of bone graft substitutes including osteoconductive and osteoinductive materials for their ability to promote lumbar spine fusion.

Presently available osteoconductive bone graft substitutes do not seem to be able to function as a stand-alone substitute for autograft in posterolateral spine fusion. These materials do have promise as bone graft extenders and carriers for osteoinductive growth factors. Presently available osteoinductive materials consist mainly of various forms of demineralised bone matrix (DBM). There is substantial variability between different brands of DBM and different formulation based on variables, which are not entirely clear. Based on experimental work with Grafton DBM in rabbits, the putty and flex form appear to have a greater bone induction response than the original gel form and a greater response than autograft – in the rabbit model.

Future osteoinductive bone graft substitutes were also reviewed including an extracted mixture of BMPs (NeOsteo, Sulzer Biologics) and a recombinant BMP (rhBMP-2, Medtronic Sofamor-Danek). These materials had much stronger osteoinductive capacity than DBM; however, selection of the appropriate carrier matrix was critical for success of bone induction in non-human primates. Preliminary results with rhBMP-2 in anterior fusion cages in humans have been encouraging and studies are ongoing.

Approval of extracted and recombinant bone growth factors is likely on the horizon for very specific clinical indications. Due to the complexity of selecting the correct dose and carrier matrix, off-label use will be extremely hazardous. If preliminary results are confirmed in larger clinical trials, the potential to exceed the success rate of autogenous bone graft with less morbidity may become a reality.

THE ROLE OF FUSION IN THE MANAGEMENT OF DEGENERATIVE SPONDYLOLISTHES

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Degenerative spondylolisthesis usually occurs after the age of 40, is most common in women (ratio women to men = 4:1) and usually involves the L4-5 interspace. Sagittal facet joint orientation may predispose for the development of degenerative spondylolisthesis, which can be regarded as secondary to long-standing, segmental instability with degeneration of disc and facet joints. The pain often involves activity-related back pain, which may radiate into one or both legs.

Conservative management should be tried in early stages, and may include physical therapy, non-steroidal anti-inflammatory medication and epidural or selective nerve root injections. Degenerative spondylolisthesis is often associated with spinal stenosis. Indications for surgery are persistent pain after adequate conservative

care. Especially, neurogenic claudication or radiculopathy are regarded as indications for surgical treatment, which usually consists of posterior decompression with or without posterolateral fusion. Indications for fusion involve considerations of patient age, disc height, degree of anterior translation, facet joint orientation and previous surgery at the same level. The role of fusion in degenerative spondylolisthesis is well established, but the indications for use of spinal instrumentation needs further clinical evaluation.

References

Garfin SR, Herkowitz HN, Mirkovic S, Booth RE. Spinal Stenosis. Nonoperative and operative treatment. In: RH Rothman and FA Simeone (eds.): *The Spine*, 3rd edition. WB Saunders Co, Philadelphia pp. 857-875, 1992.

Herkowitz HN, Kurz LT. Degenerative lumbar spondylolisthesis with spinal stenosis. *J Bone Joint Surg* 1991;73A:802.

Johnson KE, Johnell I, Udén A, Willner S. Pre-operative and post-operative instability in lumbar spine stenosis. *Spine* 1989;14:591-3.

Love TW, Fagan AB, Fraser RD. Degenerative spondylolisthesis. Developmental or acquired? *J Bone Joint Surg* 1999;81B:670.

Slosar PJ, Reynolds JB. Degenerative spondylolisthesis. In: AH White and JA Schofferman (eds.): *Spine Care Operative Treatment Vol 2*, Mosby, St. Louis, pp. 1266-1279, 1995.

CONGENITAL VERTEBRAL ABNORMALITIES AND THEIR ASSOCIATIONS

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The embryologic development of the musculoskeletal system is closely linked with all of the main organ systems. We report on a prospective series of 202 patients with congenital vertebral abnormalities and document associated abnormalities in other body systems. There were 100 males and 102 females. There were 460 associated abnormalities in 153 of our 202 patients, an average of 2.27 abnormalities per patient. An intravenous pyelogram (IVP) was carried out on 173 (85.6%) patients and the remaining 29 (14.4%) had an ultrasonographic study. Patients with genitourinary anomalies were more likely to have musculoskeletal ($p=0.002$), gastrointestinal ($p=0.02$) and cardiac abnormalities ($p=0.008$) than those without genitourinary involvement. Fifty-four patients (26.7%) had at least one genitourinary abnormality and the most frequent abnormality was unilateral renal agenesis. Evidence of obstruction was present in six (3%) patients. There was no association between place of birth (urban or rural), birth order, the level of spinal curvature and type of spinal anomaly and genitourinary abnormality. However, there was a statistically significant association ($p=0.04$) between costal and genitourinary abnormalities. This incidence and urological abnormalities of 26.7% is comparable to than in previously reported series. The diagnosis of congenital vertebral abnormalities should alert the clinician to a spectrum of possible associated anomalies, as most of these are of clinical importance.

DEGENERATIVE STENOSIS CAUSING NEUROVASCULAR COMPRESSION WITHIN LUMBOSACRAL SPINAL AND INTERVERTEBRAL CANALS

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Symptoms and signs of spinal cord and/or nerve root compression occur when abnormal tissues impinge on the spinal cord¹ or nerve roots, for example when intervertebral disc protrusion causes canal stenosis². Encroachment upon

neurovascular structures in the spinal and intervertebral canals can be due to many causes, for example overt pathology, bony and or soft tissue degenerative changes³, and axial loading causing stenosis⁴. Plain film radiographs can suggest stenosis, particularly when taken in the weight bearing position.

The objective of this paper is to describe some possible causes of encroachment upon human lumbosacral spinal and intervertebral canal neurovascular structures using imaging and histopathology sections, and to show some examples.

A review of some imaging films of patients aged 38-68 years and some human autopsy histopathological sections from 40-76 year old cadavers to determine what structures may be responsible for neurovascular compression in individuals in this age group.

Stenosis of spinal and intervertebral canal neurovascular structures can be due to various bony and soft tissue structures, eg osteophytosis of the vertebral body and zygapophysial joints, and to intervertebral disc protrusion, ossification of the posterior longitudinal ligament, and ligamentum flavum hypertrophy or buckling.

Various forms of spinal and intervertebral canal stenosis can cause compression of neurovascular structures that may, in turn, be responsible for symptomatology. Of course, autopsy findings cannot be equated to spinal pain syndromes in patients.

References

- 1 Herkowitz HN: Management of syndromes related to spinal stenosis. In *Essentials of the Spine* (JN Weinstein, BL Rydevik, VKH Sonntag (eds)), New York, Raven Press, 1995, 177-193.
- 2 Matsui H, Olmarker K, Cornefjord M, Takahashi K, Rydevik B: Local electrophysiologic stimulation in experimental double level cauda equina compression. *Spine* 1992;17:1075-8.
- 3 Spinal and intervertebral canals. In *Clinical Anatomy and Management of Low Back Pain* (LGF Giles, KP Singer (eds)), Oxford, Butterworth-Heinemann. 1997, pp 97-113.
- 4 Willén J, Danielson B, Gaulitz A, Niklason T, Schonstrom N, Hansson T. Dynamic effects on the lumbar spinal canal. *Spine* 1997;22:2968-76.

THE VALUE OF NERVE ROOT INJECTIONS IN THE EVALUATION OF SCIATICA IN PATIENTS WITH NORMAL MRI SCANS

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This is a prospective evaluation of 40 consecutive patients with sciatica who had 'Normal' MRI scans, were further investigated with Nerve Root Injections (NRI), and subsequent surgery in those who had relief of symptoms.

The objectives were to evaluate the diagnostic value of NRIs in the presence of normal MRI scans and to assess the aetiology of the sciatica.

Since the advent of MRI scans the use of NRIs has been in decline as a diagnostic tool. There has been no study in their usefulness when the MRI has been reported as showing no evidence of nerve root compression, and furthermore what the surgical findings were in the patients who went on to exploration.

Forty patients with sciatica in whom the MRI scan had been reported as showing no evidence of nerve root compression by an independent observer, had diagnostic NRIs performed. 11 of these patients had reproduction of and subsequent complete relief of sciatica. These 11 patients underwent exploratory surgery, with the patient prone maintaining a physiological lordosis.

Of the 40 patients, 25 had no benefit, four patients had permanent relief and 11 had temporary relief. These 11 patients underwent surgery. All patients undergoing

surgery were L5 nerve root explorations. In nine cases the compression was by the ligamentum flavum and in two at the foramen. Of the eleven cases operated on, nine had complete relief of symptoms and two were unchanged.

MRI scans do not show a cause for sciatica in all patients, as it is not a dynamic test. In the presence of a normal MRI scan, NRIs should be performed as a further investigation.

A METHOD TO SECURE THE ACCURACY OF DETERMINATION OF INSTANTANEOUS CENTRES OF ROTATION

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In normal spines, instantaneous centres of rotation (ICRs) fall into discrete normal locations. Abnormal ICRs occur in patients with spinal pain, and in patients with putative instability. A difficulty, however, that has bedevilled biomechanics is that the determination of ICRs is subject to errors. This is one of the reasons why the use of ICRs for research and clinical purposes has not further advanced. The present study was undertaken to develop a means of ensuring the accuracy of ICRs.

The geometry of spinal motion about an ICR dictates certain relationships the location of the ICR, and the location of the centres of reaction of the moving vertebra. If the ICR is accurately located the centre of rotation, in each view of the vertebra, will lie at the same distance from the posterior inferior corner of the endplate. Furthermore, the interval between the two locations of the centre of reaction will be parallel to the transverse plane of the vertebra. Any deviation from these ideal, correct properties indicates that the location of the ICR is not accurate. By analysing the mathematics relating the location of the ICR to the locations of the centres of reaction and the slope of the interval between them, equations were derived to relate errors (ΔX , ΔY) in the X and Y coordinates of the ICR to deviations from ideal in the location of the centres of reaction in the extension position (ΔCR_{ext}) and in the flexion position (ΔCR_{flex}).

The equations derived are:

$$\Delta CR_{ext} = [\Delta X \cdot \cos(\theta/2) / \cos(\alpha - \theta/2)] - [\Delta Y \cdot \sin(\theta/2) / \cos(\alpha - \theta/2)]$$

$$\Delta CR_{flex} = [\Delta X \cdot \cos(\theta/2) / \cos(\alpha - \theta/2)] + [\Delta Y \cdot \sin(\theta/2) / \cos(\alpha - \theta/2)]$$

where θ is the amplitude of rotation. A more complex equation relates the errors to the slope of the interval between the centres of reaction.

Using the derived relationships, an investigator can check if their determination of an ICR is erroneous or not. If there is an error in the ICR it will be evident as an inequality in the locations of the centres of reaction, and a deviation above horizontal of the interval between the centres of reaction. If $|CR_{ext}| - |CR_{flex}| = 0$, and if the slope is horizontal, there can be no error in the ICR. For typical values ranges of lumbar spine motion, if $|CR_{ext} - CR_{flex}|$ is less than 1 mm, the error in Y_{ICR} will be less than about 3 mm. If the difference is greater than 1 mm, the error in Y_{ICR} may be unacceptable. If the deviation in slope is less than 5° , the error in X_{ICR} will be less than about 1 mm. By checking their determinations in this way, and undertaking corrections when indicated, an investigator can be assured of having found the correct ICR.

ABNORMAL QUALITY OF SEGMENT MOTION, WITHOUT EXCESS HORIZONTAL DISPLACEMENT, FOUND IN CASES OF LUMBAR INSTABILITY

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The detection of abnormal segmental motion, in cases of symptomatic lumbar instability, has proved elusive. Encouraging results, however, have emerged

concerning the possible utility of studying the quality of motion of lumbar segments. The location of the instantaneous centre of rotation (ICR) reflects the quality of motion of a segment, and is a mathematical function of the magnitude of translation (T) of the moving vertebra, its rotation ($^{\circ}$), and the location of the centre of reaction (CR). The detection of abnormal ICRs may, therefore, be of use in the diagnosis of conditions such as lumbar instability, and may be both more sensitive and more specific than simply measuring absolute range of movement. The present study was undertaken to test this conjecture.

Eight consecutive sets of flexion/extension radiographs, taken over the past seven years, of patients with symptoms of lumbar instability, were examined. The same method of tracing and geometric constructions, used to determine normative data, was employed to measure the parameters of segment motion viz the ICR, CR, $^{\circ}$, and T.

In each case, at one lumbar segment, the locations of the ICRs fell outside ellipses representing the effective outer limit of normal distribution. In six cases, four at L5/S1 and two at L4/5, the values for the X co-ordinates of the ICRs were less than the lower limit of normal, displacing the ICRs posteriorly. In these cases, the posterior displacement of the ICR was due to an abnormal posterior location of the CR. Angular motion was normal, and rather increased, the translation was at the lower limit of normal (0 – 2.5 mm). In the remaining two cases, the X co-ordinates of the ICRs were normal but the Y co-ordinates at L4/5 were less than the lower normal limit, displacing the ICRs inferiorly. The locations of the CRs, and the magnitudes of translation and rotation were within normal ranges. This pattern of values arises because the patients had axial subluxation upon extension, that is, their vertebral bodies flopped downwards, indicating severe impairment of the posterior anulus.

These findings provide evidence of abnormally located ICRs in patients with symptoms of lumbar instability. The results attest to the putative diagnostic potential of abnormally located ICRs. The absence of excessive translation in these cases indicates that symptomatic lumbar instability is not related to listhesis. Rather, the abnormal locations of the centres of reaction suggest that instability involves movements about an abnormal operating point, which in turn suggests internal disruption of the intervertebral disc.

THE “FAGOT” ANTERIOR COLUMN RECONSTRUCTION GRAFT

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The surgical management of destructive anterior column lesions of the spine usually requires some kind of anterior column reconstruction. A number of prosthetic devices have been devised but they cannot provide long term fixation without biological supplementation. Most of these devices are radio-opaque and interfere with post-operative imaging. Harvesting large iliac crest autograft requires a separate surgical approach and can be associated with a high morbidity.

An innovative technique is presented for anterior column reconstruction using readily available local autologous bone, bundled together to provide a strong structural biological graft, avoiding an extra incision and its related complications. The method can be used in reconstructive procedures in the thoracic and upper lumbar spine where the approach is via thoracotomy or via an extra-pleural rib bed approach.

During the surgical approach the maximum length of rib is excised and wrapped in saline soaked swabs. After corpectomy the length of the required graft is measured and the rib appropriately divided to provide sufficient length. Usually three or four segments of rib are used. In developing the technique the ribs were initially bound together using an absorbable suture hence the name was derived (fagot – a

bundle of sticks or twigs). Unfortunately this arrangement proved to be difficult to handle and potentially unstable. Subsequently, it was found that securing the segments of rib using two fully threaded AO 3.5 mm cortical screws provided a strong and stable construct. The segments are cut to a slightly greater length than required and after assembling the fagot it is trimmed to the final length. The final construct is robust and if necessary, allows forceful manipulation and punching into position. Supplementary fixation is usually required either by way of an anterior fixation device or via a separate posterior approach with pedicle screw fixation.

To date the procedure has been used in five patients with no complication associated with the technique itself. There has been no collapse of the graft and no infection.

“Fagot” anterior column reconstruction rib graft is a solid construct. The graft material is readily available during the operative approach avoiding an extra incision and its related complications. In the short follow up, there were no significant graft related complications. Interference on post-operative imaging from the fixation screws is minimal. The procedure is recommended as a simple method that provides a strong biological construct for anterior column spinal defects.

SECONDARY SPINAL PARAGANGLIOMA

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Primary paragangliomas are rare and familial tumours¹. Secondary extradural spinal paragangliomas are excessively rare²⁻⁵. They are perhaps the most difficult spinal secondary tumour to resect as they are extremely vascular. Three cases are presented to illustrate different clinical presentations, which necessitated surgical intervention, and to describe the outcomes.

Our three patients presented at ages 10, 36 and 43 years. One patient presented with a rapidly progressive paraplegia, one had a pathological fracture in the vertebral body and the third patient had severe spinal pain, an increasingly hoarse voice and a dermatomal sensory loss. All patients were noted radiologically to have extensive bone destruction of the vertebral body. A radical debridement to beyond the tumour margin was required in all cases to stem the torrential blood flow. One patient subsequently required further surgery at the same spinal level and the others required prophylactic pinning of the proximal femur.

All patients have since died of widespread metastatic disease at 12 and 14 months and three years from initial presentation.

Having reviewed these cases and available literature on metastatic paraganglioma, we believe that a team approach to their management should be adopted. If surgical intervention is considered necessary, we believe that pre-operative angiography is prudent, followed by embolisation if the typical vascularity of the tumour is demonstrated.

1. Moran CA, Albores-Saavedra J, Wenig BM, Mena H. Pigmented extraadrenal paragangliomas. A clinicopathologic and immunohistochemical study of five cases. *Cancer* 1997;79(2):398-402.
2. Brodkey JA, Brodkey JS, Watbridge CB. Metastatic paraganglioma causing spinal cord compression. *Spine* 1995;20(3):367-72.
3. Cybulski GR, Nijensohn E, Brody BA, Meyer PR, Cohen B. Spinal cord compression from a thoracic paraganglioma; case report. *Neurosurgery* 1991;8(2):306-9.
4. Osborn RE, Mojtahedi S. Paraganglioma metastatic to the cervical spine. *Computerized Radiol* 1986;10(4):167-70.
5. Kornmann C, Tennstedt A. Malignant paraganglioma. *Zentralblatt-Allg-Pathol* 1985;130(3):205-10.

A NEW MODEL FOR LUMBAR RADICULOPATHY IN THE RAT

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This study was designed to evaluate a new rat model for lumbar radiculopathy (LR). The objective was to determine if a new model for LR in the rat using a posterolateral approach to the L5 nerve root and application of autologous nucleus pulposus has advantages over the existing models.

The pathophysiology of low back pain and LR secondary to disc prolapse remains obscure. A number of useful animal models have been developed to simulate disc prolapse and have contributed to an improved understanding of LR. In an effort to improve upon existing LR models we have developed a new model for LR: using a muscle splitting posterolateral approach to expose the L5 nerve root and enabling autologous nucleus pulposus to be harvested from the L5/6 disc and applied to the L5 nerve root.

Twenty-four male Holtzman rats (weighing 200 – 225 g at the time of surgery) were placed into one of four treatment groups. (1) chromic group (n=8) in which a posterolateral muscle splitting approach was made to the left L5/6 intervertebral foramen. Bone rongeurs were then used to enlarge the L5/6 intervertebral foramen, exposing the L5 dorsal root ganglia and nerve roots. The nerve roots were ligated loosely with chromic gut; (2) nucleus pulposus group (n=8) in which a posterolateral approach was performed and a 3 mm horizontal incision was made in the posterolateral annulus fibrosis and the spine was manipulated to produce a disc prolapse which was sutured to the L5 nerve root; (3) sham group (n=4) in which just the approach was made; (4) sham group in which approach is made and the spine was manipulated as for the nucleus pulposus group. Behavioural testing: the animals were tested for mechanical allodynia (increased tactile sensitivity) using von Frey filaments up to 42 days postoperatively. Immunohistochemistry: the L5 segments of the spinal cord were harvested at seven and 42 days postoperatively for immunohistochemical detection of glial activation.

The chromic and nucleus pulposus groups displayed similar mechanical allodynia in both the ipsilateral and contralateral hind paws. The sham groups exhibited minimal mechanical allodynia. Increased immunoreactivity was observed in both the chromic and nucleus pulposus groups indicating similar microglial and astrocytic activation.

This new model for lumbar radiculopathy using a posterolateral approach and autologous nucleus pulposus is effective in producing behavioural and immunohistochemical changes that are consistent with other models simulating lumbar radiculopathy. Advantages of this new model include: less extensive exposure, less intrusion in the spinal canal, improved access to the L5/6 disc and the utilisation of autologous nucleus pulposus as opposed to chromic gut.

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THE USE AND EARLY RESULTS OF AUTOLOGOUS GROWTH FACTOR IN LUMBAR SPINAL SURGERY

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The purpose of this report is to explore the technology and present the early results of the use of Autologous Growth Factor (AGF) to enhance lumbar fusions.

Using an intra-operative technique to harvest and concentrate the platelets, the bone healing cascade and its initiation through platelet aggregation will be explored with developmental study data presented to support the rationale for the use of AGF in the clinical setting. A retrospective review of fifty adult patients undergoing lumbar fusion surgery with AGF for degenerative disease will be presented.

The early results of the use of the AGF mixed with bone graft material appear to indicate that early bone graft healing is enhanced as manifested by a bloom of bone healing seen on one, three and six months follow up radiographs.

One of the initial results of many growth factors that have been shown to affect bone formation, including bone trauma and subsequent healing is the aggregation of platelets at the injury site. With them they bring Platelet Derived Growth Factor and Transforming Growth Factor Beta. AGF is a concentrated autologous buffy coat gel which has platelet and Growth Factor concentrations which are six – 10 times patient baseline, and induces bone growth through chemotaxis, mitogenesis and cell differentiation.

The use of AGF to enhance lumbar fusions is an exciting new technology, which is autologous, easy to handle, readily available and cost effective. Furthermore, its use is not clouded by concerns of dosage, carrier mediums, or product cost and availability.

GENE THERAPY FOR SPINE FUSION

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The gold standard graft material for spine fusion remains autogenous iliac crest bone. Autograft has limited supply, is associated with harvest morbidity, and often results in nonunion. Recombinant and extracted forms of bone morphogenetic proteins (BMPs) will soon become available. These proteins are relatively expensive and have not yet been tested in a wide range of clinical applications for consistency of response. A number of laboratories are experimenting with delivering the gene encoding for an osteoinductive protein rather than the protein itself. The purpose of this paper is to introduce this concept and to review the existing literature of gene therapy spine fusion projects and to describe progress with a novel gene therapy project.

We have identified and cloned a novel osteoinductive cDNA name LIM Mineralization Protein-1 (LMP-1) which is expressed very early during membranous bone formation *in vitro* and *in vivo*. Experiments have been undertaken to deliver this cDNA using a variety of approaches to evaluate its ability to induce bone formation *in vitro* and *in vivo*.

In vivo experiments were performed to determine if adenovirus containing the LMP-1 cDNA could promote lumbar spine fusion in skeletally mature New Zealand white rabbits. In a pilot study, 3 ml of bone marrow was aspirated from the distal femur; the buffy coat was isolated and transduced for 10 min with AdV. Single level bilateral posterolateral lumbar spine arthrodesis was performed and carrier matrix (rabbit devitalised bone matrix or collagen sponge) was implanted with each side containing $8-15 \times 10^6$ buffy coat cells transduced with either AdLMP-1 (MOI=0.4 or 0.04) or Ad \square gal (MOI=0.4). After five weeks, all spine fusion sites that received AdLMP-1 (MOI=0.4) contained solid, continuous spine fusion masses. In contrast, sites receiving Ad \square gal or the lower dose of AdLMP-1 did not form solid fusion mass bone. A pivotal study was then performed (n=20) with several enhancements to the technique: (1) peripheral venous blood was used as a cell source instead of marrow; (2) the carrier matrix was switched to a collagen/ceramic composite sponge to prevent premature resorption; and, (3) the control cells received empty adenovirus

rather than the β -gal transgene. All 10 rabbits that received AdLMP-1 had solid spine fusions as determined by manual palpation, x-ray, CT scan, and biomechanical testing. In the 10 rabbits that received cells transduced with the empty adenovirus, little or no bone was formed. Histology confirmed that the bone formed was normal primary trabeculae with active osteoblasts and marrow elements.

Adenovirus delivery of transgenes *in vivo* has been limited by immune response to the virus, toxicity from high doses, long transduction times, and inconsistent results. We showed consistent bone induction in a challenging spine fusion model. Intraoperative *ex vivo* gene transduction (10 min) of venous blood cells is easier than other protocols that require overnight transduction, cell selection, or cell expansion in culture. The dose of virus (MOI=0.4, 5×10^8 viral particles) was substantially lower than in most other gene therapy applications. The low dose required may be due to the fact that LMP-1 is an intracellular molecule and may induce potent signal amplification cascades.