Toward a cure for lumbar spinal stenosis: The potential of interspinous process decompression

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A B S T R A C T

There is a growing impetus to treat aging as a disease in the quest to significantly extend the human life span through cellular regeneration methods. This approach, while promising, overlooks the fact that the evolutionary adaptation to bipedalism puts the human body in a distinctively vulnerable biomechanical and functional position. Orthograde human posture places unusually-high axial compressive loads on the weight-bearing joints of the skeleton, resulting in arthritic deterioration with aging. The effects are particularly robust in the lumbar spine where age-related degeneration, most commonly lumbar spinal stenosis (LSS), is ubiquitous among the elderly. It is postulated that re-establishing a favorable mechanical environment via interventions that unload the affected spinal joint complex may mitigate and potentially reverse the structural damage that is the cardinal pathoanatomical feature of this disease. The hypothesis of this paper is that a minimally-invasive surgical procedure, interspinous process decompression (IPD), which utilizes a stand-alone intervertebral spacer, effectively unloads the diseased spinal motion segment providing a healthy micro-environment to reverse and repair age-related and genetic deterioration of the spinal motion segment. Several lines of supporting evidence are provided from long-term follow-up results of a randomized controlled trial of IPD safety and effectiveness of the Superion® device including clinical outcomes, reoperation rates, opioid analgesic usage and advanced imaging utilization. All of these outcomes show uniquely-favorable trends with time that imply that the benefits of IPD are structural. The compendium of evidence suggests that IPD offers both a durable palliative effect due to direct blocking of back extension and a disease-modifying effect due to unloading of the spinal joint complex.

Background

Despite the tremendous accomplishments that modern medicine has achieved in defeating an impressive list of diseases, in developing potent biopharmaceuticals and effective devices, in elucidating pathology with advanced imaging, and in unraveling the human genome, humans continue to suffer from the inevitable ravages of aging and the chronic illnesses that accompany this process [1]. However, researchers on the “cutting edge” of medical technology advancement envision breakthroughs that would effectively double life expectancy to 150 years or longer [2]. These futurists have as their core paradigm that aging itself should be treated as a disease [3]. And, by extension, prolonging life presumes that chronic age-related diseases can be cured [4].

Most proposed rejuvenation technologies employ a “turn back the hands of time” approach that seeks to biologically revert senescent cells to youthful, healthy cells [5]. While cellular regeneration has shown early promise as a means of reversing markers of aging in animal models, it ignores the distinctive morphoanatomical features of the human body that predestine to chronic, structural degeneration of the musculoskeletal system. Indeed, nearly 7 million years ago our ancestors initiated the evolutionary journey toward habitual orthograde human posture and bipedal locomotion [6]. This singular and uniquely-human characteristic, which preceded the development of the large brain by millions of years, may have been perhaps the most salient trigger of all the traits, such as cognizance and language, that collectively and ultimately define humanity. Accepting upright bipedalism as a seminal human feature does not forgive that this evolutionary adaptation puts the body in a distinctively adverse biomechanical and functional position [7]. Standing and ambulating with an upright posture places unusually high axial compressive loads on the weight-bearing joints of the skeleton, resulting in arthritic deterioration with aging.

It is now generally recognized that onset and progression of this arthritic deterioration is mediated largely through biomechanical forces acting across the joint and the failed repair of damage caused by excessive mechanical stresses and repetitive loading on joint tissues [8]. Specifically, intra-articular stress secondary to subfracture impulsive loading culminates in micro-injury of subchondral bone and articular cartilage which, when applied repetitively, can exceed the ability of the joint to repair the damage.

While axial loading associated with bipedalism is an accepted antecedent to osteoarthritis of the synovial joints of the lower
extremities, the effects may be most profound in the spine, particularly the lower vertebrae [9,10]. In fact, the S-shaped sagittal profile of the human spine, an adaptive anatomical feature not present at birth, results from biomechanical forces exerted on the spine from bipedalism. In contrast, our closest phylogenetic relatives, the great apes, possess a relatively stiff and straight spinal column with evenly spaced vertebral bodies adapted to quadrupedal movement. As a result, humans, with their widely curving, flexible spines, display substantially more degenerative and traumatic spinal pathologies than non-human primates [11,12]. This has led some investigators to hypothesize that our unique mode of locomotion, bipedalism, may influence the development of these conditions [9,13]. Recent research has shown that not only does vertebral shape differ between humans and great apes, but human vertebrae showing age-related deterioration are closer in shape to apes than to healthy humans, suggesting that they were morphologically less well adapted to upright posture [14]. Additional research is required to elucidate whether human spines with less curvature are associated with a reduced risk of degenerative changes.

The human evolutionary adaptation of a curved and flexible spine which allows hyper-extension results in almost ubiquitous imaging-evidence of spinal deterioration among elderly adults, irrespective of whether they exhibit clinical symptoms [15,16]. In contrast to hip and knee osteoarthritis which are not universal clinical phenomena in older individuals, retaining a healthy, youthful spine into old age is virtually impossible. Thus, any realistic attempt to significantly extend the human life span would require that age-related spinal degeneration be not only markedly attenuated, but likely reversed.

The hypothesis of this paper is that a minimally-invasive surgical procedure, interspinous process decompression (IPD), which utilizes a stand-alone intervertebral spacer, effectively unloads the diseased spinal motion segment providing a healthier micro-environment to mitigate and possibly reverse and repair age-related arthritic damage.

Pathoanatomical features of lumbar spinal stenosis

Lumbar spinal stenosis (LSS) is the end-product of decades of compressive forces acting on the spine [17,18], and remains the most common indication for back surgery in the elderly [19]. No portion of the spinal motion segment’s three-joint complex, consisting of two facet joints and the intervertebral disc, is spared the age-related degeneration caused by repetitive axial loading [15]. Consequently, LSS consists of a mosaic of pathoanatomical features including classic synovial joint osteoarthritis of the facet joints [20–22] often coupled with more widespread osseoligamentous deterioration such as ligamentum flavum hypertrophy and buckling, varying degrees of disc-associated impingement, as well as spur and osteophyte formation [16,23–25].

Traditionally, the anatomical classification of LSS includes three types of stenosis: central canal, lateral recess (sub-articular), and foraminal (Fig. 1). In central canal stenosis, the spinal canal is constricted at the affected intervertebral level by ligamentum flavum buckling or hypertrophy, disc protrusion, hypertrophic facet joints, and degenerative spondylolisthesis causing compression of the spinal cord or cauda equina [26]. On magnetic resonance imaging, epidural fat is mostly obliterated. The cauda equina can be compressed anteriorly due to disc protrusion and/or posteriorly by hypertrophic facets and ligamenta flava [16].

Lateral recess stenosis involves the tubular canal that acts as the conduit through which the nerve roots exit. The entrance zone or lateral recess of the nerve root canal is most commonly compressed by hypertrophic osteoarthritis of the facet joint, particularly involving the superior articular process. Additionally, narrowing of the lateral recess can result from posterior disc protrusion, which compresses the nerve root as it emerges from the dural sac [16].

Stenosis can also occur in the exit zone or neural foramen of the nerve root canal, i.e., foraminal stenosis. In addition to hypertrophic osteoarthritic changes in the facet joints, osteophytic ridge formation along the superior margin of the disc serves to reduce the foraminal aperture, thereby impinging the exiting nerve [16].

Given these complex anatomical considerations, LSS can be a debilitating degenerative condition due to its intimate contact with important neural structures including the cauda equina of the spinal cord and the nerve roots and exiting nerves. Compression of the spinal cord from central canal stenosis elicits the cardinal clinical symptom of LSS, neurogenic claudication. This often presents concurrently with radiculopathy from lateral recess and foraminal encroachment [27].

LSS has an important dynamic component. The degenerative anatomical changes render neurovascular structures vulnerable to mechanical compression during lumbar extension, producing the classic neurogenic claudication and radicular symptoms of LSS. The available space in the central spinal canal decreases in loading and extension and increases in axial distraction and flexion [28]. The same dynamics also affect the foramen with flexion causing a 12% increase, and extension a 15% decrease, in surface area [29]. Thus, a distinguishing clinical attribute of neurogenic claudication is its relationship to the patient’s posture where lumbar extension increases and flexion decreases pain onset and severity. Symptoms progressively worsen when standing or walking and are relieved by sitting or bending forward to mimic, ironically, a pre-evolutionary simian stance.

The pathoanatomical features of spinal degeneration are necessary but not sufficient for symptomatic LSS. These features are also present in high proportions of asymptomatic individuals, increasing with age. Many imaging-based degenerative features are likely part of normal aging and unassociated with pain [30]. Consequently, characteristics of spinal degeneration are almost universal among the very old underscoring the salience of this issue in efforts to substantially extend the human life span.

Interspinous process decompression

Interspinous process decompression (IPD) devices (“spacers”) were developed to build on the concept that back extension is a seminal factor in the causative chain that instigates neurogenic claudication in LSS. Spacers provide immediate symptom amelioration by serving as a spinal extension blocker to prevent the repetitive compression of neurovascular elements during back extension that is the primary source of neurogenic claudication and radicular symptoms. The Superior® Indirect Decompression System (Vertiflex, Carlsbad, CA USA) represents a second-generation IPD device and is the only commercially available device in the US (Fig. 2).

Spacers are inserted posteriorly via a minimally-invasive procedure without disruption of osseous or ligamentous tissues [31]. They are implanted in a stand-alone manner without the need for concomitant surgical decompressive laminectomy. The device is inserted through a
cannula, and under fluoroscopic guidance is deployed between adjacent vertebral spinous processes at the indicated level. The insertion instrumentation is then removed, leaving the implant in place. The rigid implant maintains the desired spacing between the spinous processes while still preserving motion (Fig. 3). This maintains the intervertebral space and prevents narrowing of the canal and neuroforamen by limiting extension at that level. Spacers can also be removed if necessary via a minimally-invasive technique that also causes no anatomical disruption.

Reversing skeletal degeneration: the concept of joint unloading

It has been over four decades since renowned orthopedic surgeon, Professor Eric L. Radin, first advanced the now-accepted theory that arthritic degradation and progression, particularly of the large synovial joints, was principally facilitated through failed attempts at subchondral bone and cartilage repair secondary to excessive mechanical loading at the joint [32]. In his 1984 ambitiously-titled commentary *Hypothesis: joints can heal*, Radin postulated that repetitive impulse loading causes microfractures to develop in the subchondral endplate, resulting in local osteoporosis, subchondral sclerosis, and subsequent cartilage degeneration [33]. He argued that joint repair should be the goal of therapy since emphasis on cartilage regeneration alone does not address the underlying damage and remodeling of subchondral bone that persists under the abnormal mechanical conditions inherent in arthritis. He posited that it is unlikely that structural integrity and clinical outcomes will be durable if the joint remains in the same adverse mechanical environment that produced the nascent conditions for arthritis to develop and progress [34].

Radin took the hypothesis one step further and contended that if the pathological stress pattern across the joint is normalized, extrinsic cells can induce repair by forming fibrocartilage, remodeling of the subchondral plate to a typical trabeculated pattern will ensue, regaining its shock absorption quality and joint space width will be re-established [33]. Over the long term, competent hyaline cartilage may re-form if the load distribution is durably maintained [35].

Waller at el [36] recently revived the joint unloading theory as a proposed means of countering the persistent effects of axial loading on arthritic joint degeneration. They noted a growing body of supporting
evidence for interventions specifically focused on joint unloading. For example, a number of studies have found that knee joint distraction using an external fixator for a period of 2 months resulted in sustained structural improvements and regenerated cartilage in cases of severe osteoarthritis [37–39]. Thus, direct unloading of the joint with distraction re-establishes a favorable local mechanical environment eliciting a disease-modifying effect by attenuating secondary inflammation, cartilage degeneration and subchondral bone remodeling due to the absence of mechanical loading [40].

While knee distraction, although surgically rudimentary, provides proof of concept for the potential of joint unloading in repairing arthritic damage, its surgical invasiveness limits its widespread application. To circumvent this limitation, Miller et al. [41] reported that a minimally-invasive, knee joint unloading device has shown quantitative imaging confirmation of subchondral bone healing after 2 years, a \textit{sine qua non} for re-establishing a healthy joint.

Early evidence suggests that the hypothesis of Radin and the encouraging findings for the potential of joint unloading in the repair of arthritic damage can be extended to the age-related deterioration that occurs in the spine with LSS. Using a sham-controlled animal model, Krooher et al. [42] and Guhering et al. [43] confirmed that disc degeneration results from hyper-physiologic vertebral loading, but that subsequent joint distraction and unloading restored disc height as well as induced tissue recovery at the cellular level. These findings were subsequently corroborated by Hee et al. [44] who noted the regeneration of the extra-cellular matrix in both the vertebral endplate and the recovery of vascular channels following disc unloading. It has been hypothesized that axial compression effectively impairs disc nutrition leading to classic features of disc degeneration. Under these conditions it is unrealistic to believe that biological interventions alone, such as gene or cellular therapies, will be successful in restoring spinal joint health. Additional research using advanced imaging is needed to evaluate whether the distraction and unloading features of an IPD device can measurably improve disc degeneration and other components of joint pathology at the affected vertebral motion segment.

Treating LSS with interspinous process decompression: core evidence

In the initial stages of IPD development, cadaveric studies with the first generation IPD device showed that the implant significantly increased spinal canal area by 18%, the sub-articular diameter by 50% and the foraminal width by 41% in extension [45]. Increases in spinal canal area have not been reported in clinical trials but are assumed to occur as a result of a similar mechanism of action. The cadaveric findings were \textit{prima facie} evidence that the underlying mechanism of action is indirect decompression of the spinal cord and nerve roots that leads to immediate symptom amelioration. Somewhat overlooked in the enthusiasm surroundings these findings was a companion cadaveric study showing that IPD also significantly reduced the compressive loads acting across the facet joints and posterior annulus during back extension [46]. So in addition to the palliative effects resulting from increased canal dimensions via extension blocking, we hypothesize that the unloading component provided by IPD may, in the end, be the most advantageous feature of this intervention by providing a beneficial disease-modifying effect. Indeed, in treadmill testing of LSS patients, Oguza et al. [47] found that loading and unloading maneuvers were more predictive of initiation of first symptoms of neurogenic claudication and total walking time than flexion and extension maneuvers.

Examining findings from a US Food and Drug Administration, Investigational Device Exemption (IDE) trial of the Superion® device (NCT00692276) [48] offers several lines of evidence to support the hypothesis that IPD alleviates deleterious compressive forces acting across the diseased spinal motion segment and effectively provides a healthy micro-environment to support the reversal and repair of age-related arthritic damage in LSS.

Clinical outcomes

The genesis of the concept that an implant placed between the spinous processes might provide relief for patients suffering from neurogenic claudication came about from a straightforward clinical observation; most of these patients get relief of symptoms when they bend forward and flex their spines and conversely their symptoms worsen when they stand erect and extend their spines. The clinical efficacy of this concept has been established at numerous annual follow-up intervals after implantation with the Superion® device [49,50]. Nunley et al. [51] reported that at five years, 84% of LSS patients treated with IPD demonstrated clinical success on at least two of three Zurich Claudication Questionnaire domains, and that 75% of patients continued to realize a clinically significant benefit in leg pain. Moreover, IPD patients achieved a 49% improvement in quality of life outcomes at five years, ameliorating the significant impairment in physical well-being found in older patients with LSS [52].

Reoperation rates

In the Superion® IDE trial, Nunley et al. [51] reported that of the 190 patients randomized to receive Superion® treatment, 142 (75%) were free from reoperation, revision, or supplemental fixation at their index level at five years. Importantly, of the 48 patients that required reoperation, 38 (79%) underwent the procedure within the initial two years of postoperative observation. Of the remaining 10 reoperations, only one occurred during the fifth year of observation suggesting a decreasing risk of revision surgery with time (Fig. 4). Using statistical

Fig. 4. Annual prevalence rates for reoperations, opioid usage and advanced imaging utilization following Superion® implantation.
modeling based on the Kaplan-Meier survival and failure rates, we have extrapolated an estimated 10-year cumulative failure rate of only 36.5% after IPD.

The decreasing risk of revision surgery with time and the predicted high IPD implant survival rate of 63.5% at 10 years may suggest that this result is a surrogate marker for repair of the spinal joint complex. This notion is supported, in part, by observation of an opposite trend in revision rates after decompressive laminectomy, the gold standard surgical treatment for LSS, which shows increasing risk of revision surgery with time [53,54]. Decompressive surgery does not arrest the surgical treatment for LSS, which shows increasing risk of revision rates after decompressive laminectomy, the gold standard high IPD implant survival rate of 63.5% at 10 years may suggest that 36.5% after IPD.

We have consistently sustained and durable through five years following IPD. These patients fail to exhibit clinical signs or complaints, such as neurogenic claudication, and they no longer have the diagnostic characteristics necessary to meet the clinical definition of LSS [60].

• The reoperation rate after IPD has a steep downward trajectory with time, with most revisions clustered within the first two years of surgery. This trend is the opposite of that observed after decompressive laminectomy and suggests that if symptom relief is not prompt after IPD, a more invasive surgical option is pursued. Over time, however, in those that realize prompt symptom relief, the unloading effects of IPD support a healthy joint complex where additional surgical decompression is not required. With laminectomy, the joint complex suffers arthritic deterioration unabated.

• LSS selectively affects older individuals and the natural course of disease is one of chronic skeletal degeneration requiring continual analgesic use and an increased utilization of advanced imaging whether managed conservatively or with decompression surgery. By addressing a putative cause of LSS pathology, the unloading feature of IPD may be its most salient attribute, providing a healthy biomechanical micro-environment to support joint repair.

Opioid use

Commensurate with the durability of symptomatic clinical improvement and decreasing risk of revision surgery noted above, Nunley et al. [56] recently reported that IPD is associated with a reduction in opioid analgesic use, from a prevalence of approximately 50% at the time of surgery to 13.3% at two years and to 7.5% at five years (Fig. 4). This finding is notable as LSS patients treated conservatively may not be expected to experience such a dramatic drop in opioid usage as the disease progresses. For example, in a randomized trial of repeated epidural steroid injections for LSS, Friedly et al. [57] reported a baseline opioid usage prevalence of 38% which increased to 41% at one year. Additionally, in a randomized controlled trial, Schmidt et al. [58] reported a pre-study opioid usage prevalence of 31%, spiking post-surgically to 67% then decreasing to 19% at one year and 23% by two years following laminectomy. Clearly, the trajectory of a steep reduction in the prevalence of opioid use after IPD reflects a unique trend that contrasts with that seen in LSS patients treated conservatively or with decompression surgery.

Imaging utilization

Reappearance of neurogenic claudication symptoms in LSS patients post-surgically often necessitates utilization of advanced imaging such as computed tomography and magnetic resonance imaging to assist in pinpointing the source of new or recurrent symptoms as well as to plan for subsequent revision surgery if necessary. Inspection of Fig. 4 shows that the annual prevalence of advanced imaging utilization decreases from 11% during the first postoperative year to about 4.5% during the fifth year after IPD. This finding is starkly dissimilar to trends in advanced imaging utilization observed after decompressive laminectomy. In a large observational study using an administrative database involving almost 50,000 patients having decompression surgery for LSS, Patel et al. [59] reported 37% of patients had a follow-up MRI within two years of surgery, with this rate rising to 55% through five years.

Evidence synthesis

Patients with chronically bothersome LSS in their eight decade of life or older should not be expected, by and large, to demonstrate clinically significant symptomatic improvement with conservative management alone. The following points synthesize the evidence that IPD may, in addition to its demonstrated palliative effects, provide a disease-modifying effect resulting in the repair of musculoskeletal degeneration and the healing of LSS.

• Clinically significant improvements in all LSS symptoms have been

References


