Form 3

Abstract of Thesis

Name	（MASNI AZIAN BINTI AKIAH ）
Title	Computational Biomechanics Study on Nerve Root Impingement due to Intervertebral Disc Degeneration (椎間板変性による神経根圧迫に関する計算バイオメカニクス研究)

As the primary function of the nervous system is to transmit signal between the brain and different body parts, any interruptions to the system may stimulate pain and affect significant body function while potentially establish pain irradiation towards lower body parts. In clinical perspective, biomechanical responses of the nervous system are primarily influenced by mechanical changes of the intervertebral disc (IVD). Such changes alter its structural characteristics as well as the postural state of the spinal unit. Interruptions to the neural element are triggered and may influence its trajectory. The relationship between different cases of IVD degeneration and its affect to the nervous system is not fully understood as data collection in clinical environment usually involves painful and invasive procedure. Development of computational model of the spinal system with the neural element offers an alternative to improve current understanding of IVD degeneration towards increased risk of nerve root interruption. However, developing the finite element (FE) model of the IVD itself is challenging as it is composed of varying combination of constitutive elements including composites of fibrous tissue with layers of alternating fibers with regional variation and gelatinous nucleus pulposus. Geometric parameters also affect the corresponding spinal behavior, which may further complicate the optimization process of a subject-specific model. Generalization to the FE model may restrict the prediction of the IVD behavior, while explicit description increases the simulation run-time.

As an alternative to this problem, systematic parameter calibration of the material nonlinearities in an IVD model using statistical factorial analysis was proposed. The calibration factors were controlled by introducing specific range of calibration parameter for the following constitutive elements; (i) annulus ground substance material coefficient and annulus fiber stiffness at the (ii) posterior, (iii) posterolateral, (iv) lateral, and (v) anterior regions. By adapting the $L_{16}(4^5)$ orthogonal array, the influence of each constitutive elements of the IVD towards the biomechanics of the spinal unit for an increasing loading has been identified. The array stipulates for different sets of material parameter combinations for sixteen simulation trials. It was found that the highest influence to the spinal motion was contributed by the annulus ground substance nonlinearity, while fiber stiffness at the anterior and lateral region affected extension and lateral bending respectively. Based on these results, the optimum combination of calibration parameters was achieved using a factorial additive model. The results from the calibrated IVD model significantly reduces computational gap of the spinal responses to *in vitro* data, which improves computational confidence to the established FE model.

From the calibrated IVD model, regional material degradation was then proposed to simulate for different cases of IVD degeneration. Degeneration factor was introduced to respective constitutive elements to simulate for varying grades of IVD degeneration including fibrous nucleus, increased fiber and ground substance laxity, increased fiber stiffness and total annular fracture along posterior and posterolateral regions. Simulation results suggested that fibrous nucleus with absence of intradiscal pressure increases the spinal instability in all primary directions. The computed bulging displacement and shear strains were particularly high for IVD with ground substance laxity and total annular fracture. Furthermore, high shear strains distributions at degenerated region suggested that fractured area were susceptible to projection of disc-bone separation.

Morphological changes to the IVD which affect the nerve root function have become the main interest of this study. To address the response of the nervous system for different states of IVD degeneration, development of the computational model adapting the degenerated IVD models with adjacent neural element were proposed. Several assumptions including utilization of a rigid body connector between the spinal unit and the adjacent neural element were introduced to simulate for actual physiologic condition. The computational simulation suggested that degenerated IVDs with extended bulging were linearly correlated to the epidural pressure. IVD with total fracture and ground substance laxity were likely to affect the motor function from the cauda-equina bundle. Lower upper body weight which corresponds to 500 N axial compression yielded highest magnitude of epidural pressure (100.8 mm Hg) when subjected to extension loading. However, as the upper body weight increases further, the rate of pressure increment were more drastic for flexion, followed by asymmetrical loadings and extension. Pressure variation may be influenced by the changes of the outer layer surface tautness of the neural element for different postural states. In addition, high pressure localization ($\geq$ 118 mm Hg) was also computed for the innervating nerve branch, nerve root region below the vertebrae pedicle, and the exiting nerve through the intervertebral foramen. An interesting phenomenon was captured during asymmetrical loading, by which the nerve root was kinked during the descendent of the upper vertebrae element. The proposed model gave an insight of the neural element mechanics for degenerated IVDs subjected to postural loads.

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論文審査の結果の要旨及び担当者

氏　名　（ MASNI AZIAN BINTI AKIAH ）	
論文審査担当者	（職）　　　　氏　名 主 査　　教　授　　田 中 正 夫 副 査　　教　授　　和 田 成 生 副 査　　教　授　　出 口 真 次

論文審査の結果の要旨

脊柱の構成要素である椎間板の変性による神経根圧迫は、神経系における信号伝達阻害要因の一つである。変性椎間板による神経根圧迫は一次的には力学的な干渉であり、椎間板変性を伴う脊柱姿勢が神経根圧迫とどのようにかかわるかについての知見は必ずしも十分ではない。しかしながら椎間板・神経根における力学状態の生体内観察は著しく困難であることから、力学モデルに基づく計算バイオメカニクスのアプローチの貢献が期待されている。本論文ではまず、異なる線維配向を有する層構造組織である線維輪とゼラチン状の髄核との複合体構造を直接に表現する詳細な構造形態モデルならびに有限要素近似によるその計算力学モデルを構築している。椎間板の複雑な非線形力学特性を表現するモデルパラメータを、実験計画法を援用する最適化プロセスとして生体内・生体外観察データにもとづき適切に行う設定する方法を提案し、第４・第５腰椎間正常椎間板を対象にその妥当性を検証するとともに、脊柱構造単位の運動への影響は線維輪基質の非線形特性が大きく、前側方向線維剛性が脊柱側屈特性に重要であることを示している。つぎに、このように構築した椎間板の計算力学モデルのコンポーネントそれぞれの変性要因を考慮することで、変性部位における特性変化や損傷に応じた局所的椎間板変性モデルを表現し、脊柱構造単位の運動が椎間板形状の変形・ひずみに及ぼす影響について考察している。さらに、椎間板変性により形状変形をおこした椎間板と隣接する神経束との相互作用について、局所的変性による変形を伴う椎間板の馬尾神経束・神経根領域への圧迫解析を通じて、椎弓根下神経根領域等への圧迫局在化を示唆している。以上のように本論文は、複合体としての構造にたいする詳細な計算力学モデルを提出するとともに、椎間板変性による神経根圧迫に関する計算バイオメカニクス解析により有用な知見を得ており、博士（工学）の学位論文として価値のあるものと認める。