Mechanical behaviour of the intervertebral disc under sustained compressive loading

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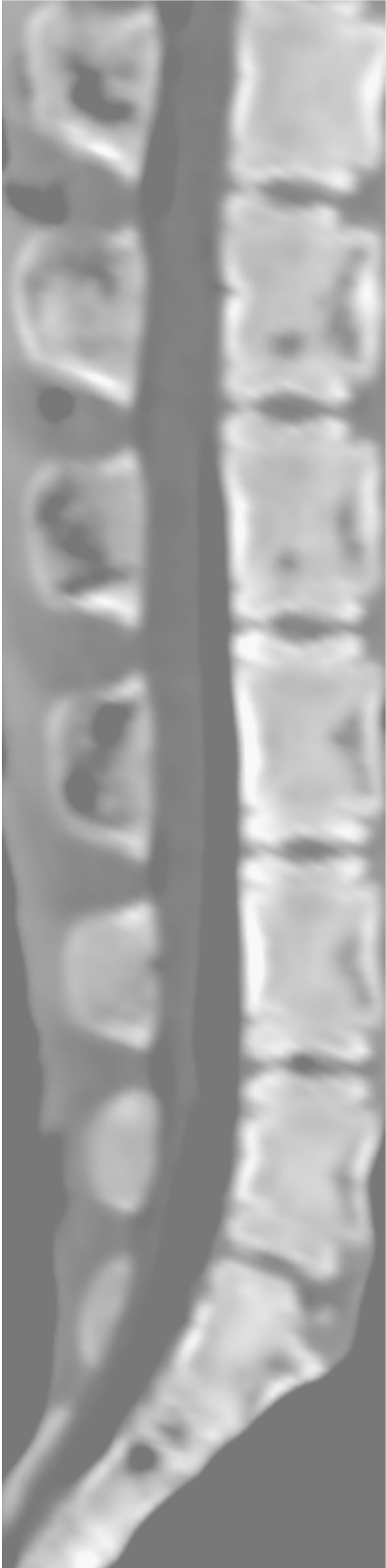
SUMMARY



The spine is a flexible structure that gives support to the upper body while providing freedom of movement to the trunk. The intervertebral disc serves as an elastic hinge between two vertebral bodies and provides flexibility to the spine. The disc comprises of the nucleus pulposus, the annulus fibrosus and the superior and inferior endplate.

The nucleus is a gelatinous structure, which consists of proteoglycans and collagen fibres, but mainly (up to 80%) of water. The chemical composition of the disc changes with age. The water content of the nucleus, however, also depends on the loading history of the disc.

The annulus fibrosus encapsulates the nucleus pulposus in its centre. It is a ring-shaped, layered structure of collagen fibres. All fibres in the same layer are parallel to each other. Each fibre runs at an angle of approximately 60° from endplate to endplate (the angle varies between 40° and 70° degrees). From one layer to the next the orientation of the fibres switches from approximately +60° to –60°.

Finally, the endplates enclose the nucleus at the top and bottom, separating the intervertebral disc from the vertebral bodies. The endplate is a perforated plate of bone with on top a layer of cartilage. The fibres of the annulus are anchored in the endplates.

The weight of head and trunk, but in particular the loads of back and abdominal muscles cause mechanical loading on the spine. The dominant loading type on the spine is axial compression. External loading on the spine leads to an increased hydrostatic pressure in the nucleus and to tension in the fibres of the annulus. The layered structure of the annulus with its alternating fibre direction is ideal for containing the hydrostatic pressure, while the flexibility in flexion/extension direction is maintained.

The osmotic pressure of the nucleus gives the disc the ability to withstand external loads. The negatively charged proteoglycans in the nucleus can attract and retain water. The percentage of water in the nucleus also depends on the external load. An increased hydrostatic pressure leads to a decreased amount of water in the nucleus and consequently to an increased difference in osmolarity relative to the environment. Fluid continues to flow out of the disc until the external load is balanced by the osmotic pressure of the nucleus. Simultaneous with the fluid flow fibres of the annulus are stretched. As a result the intervertebral disc loses height. The mechanical behaviour of the disc is poro-elastic and visco-elastic. Thus mechanical properties of the disc are non-linear and strongly time dependent.

In literature, mechanical behaviour of the disc is often described from short-term experiments, usually with the unloaded situation as a starting point. The effect of loading history on disc mechanics is, in general, disregarded. This gap in knowledge on disc behaviour under sustained loading is the starting point of the research in this thesis.

The aim of this thesis is to elucidate the role of loading history on the mechanical behaviour of a spinal segment in general, and the intervertebral disc in particular.

After a general introduction, the second chapter of this thesis addresses the difference in mechanical behaviour of a motion segment and its separate components during axial compression. Intervertebral discs, vertebrae, motion segments without posterior parts and samples of the trabecular bone of the vertebral body (both with and without endplates) were subjected to a repeated compression test. Each of the three loading cycles consisted of a loading phase (2.0 MPa, 15 minutes) and a recovery phase (zero load for 30 minutes).

Bone samples without endplates showed almost instant deformation, followed by a marginal creep (time constant approximately 0.02 minutes). With a time constant of approximately 0.25 minutes samples with the endplates attached showed a much larger creep. The largest time constant and change of specimen height were found in the creep of the intervertebral discs (time constant approximately 1 hour).

The marginal creep of bone samples shows that the role of bone in the creep behaviour of a disc is limited. However, bulging of the endplate into the vertebral body is a significant factor during the initial phase of the test.

Each component plays a distinct role in the time dependent behaviour of a motion segment. The optimal configuration for mechanical testing of motion segments is therefore the intervertebral disc with both half vertebral bodies attached, *i.e.* without the outer endplates.

In the third chapter of this thesis is shown that the mechanical response of a disc, subjected to a repeated loading cycle is asymmetric, *i.e.* changes in disc properties occurring during the loading phase are not fully restored during unloading. This seems to contradict the observations *in vivo* that loss of disc height is fully restored during recovery in spite of the fact that the duration of the loading time exceeds the duration of recovery (16 hours of daily activity vs. 8 hours of sleep). The recovery phase (zero load, 30 minutes) in the experiment of chapter 3 was -unlike the *in vivo* situation- twice as long as the loading phase (2.0 MPa, 15 minutes). Yet disc height did not recover during unloading. Also the nucleus pressure, which decreased during the subsequent loading phases, showed no full recovery during unloading, indicating that the osmotic pressure in the nucleus did not recover.

These results induced us to hypothesize that the flow rate through the endplate was smaller for fluid going into the disc than out of the disc. Obstruction of the endplate route by blood clots was thought to be responsible for this discrepancy.

All the applied loads in the previous chapters were static loads. *In vivo* loading, however, has a dynamic nature. Chapter 4 addresses fluid flow through the endplates and the effect of loading type on recovery of disc properties. To this end, the samples were divided into four groups of intervertebral discs. Two groups were subjected to static loads (three loading cycles with a nucleus pressure of 2.0 MPa. each followed by a recovery phase). The other groups were subjected to dynamic loads (three loading cycles with an average nucleus pressure of 2.0 MPa, frequency of 0.5 Hz, each followed by a recovery phase). In the second part of the test, after the static or dynamic loading protocol, the endplates were blocked with silicon paste in half the number of discs of, while the endplate was left open in the other half. The test was restarted with an extra static or dynamic loading cycle, which was followed by a 10-hour long recovery period.

During the first part of the test, all samples showed a loss of disc height coinciding with an increase in disc stiffness. There was no difference in the change of disc properties between the statically and dynamically loaded groups. The expectation was that during the second part of the test, the recovery of the group with blocked endplates would be different from the group with open endplates. However, in spite of blocking one of the routes for fluid flow of the disc, no significant difference in recovery was found. Full recovery was measured for all parameters studied after long-term unloading. The required recovery time until full restoration was long compared to the loading time. This suggests that inflow of fluid into the disc is slow compared to outflow and contrasts with the *in vivo* observation that 8 hours of recovery suffice to compensate 16 hours of loading. Furthermore, the role of the endplate route for fluid flow seems to be limited. These findings were interpreted as an indication that the validity of *in vitro* models of the disc is limited.

In order to further investigate the differences between flow behaviour into and out of the disc, an experiment was designed in which the visco-elastic and poro-elastic behaviour were uncoupled. The experiment of chapter 5 was divided into three separate test phases. In the first phase, the disc was given the opportunity to reach equilibrium with an external load (static compression: 150N, 300N, 600N or 850N). During this mechanical phase fluid was pressed out of the disc while at the same time the annulus fibres were stretched. At the start of the second phase of the test, the osmolarity of the environment was lowered (24-hours). The external load was maintained on the disc throughout the entire test. This change in osmolarity gave rise to an increase in disc height. Since the applied load was constant, this increase in disc height can only be explained by inflow of fluid. At the start of the final 24-hours of the test, the osmolarity of the environment was changed back to the initial value, again without changing the external load. Due to this increase in osmolarity, the change in height was reversed.

The time constant of the change in height was calculated for each test phase. The intervertebral disc lost height rapidly on the first day (time constant approximately 1 hour), slowly regained height on the second day (time constant approximately 8.6 hours) and finally lost height again on the third day (time constant approximately 7.2 hours). The time constant for fluid flow into the disc was larger than for the reversed flow direction. The changes in height on the second and third days were related to the applied load; the larger the applied load, the smaller the change in height.

The large difference in time constants between adaptation to mechanical loading and osmotic differences suggests that two different processes drive the mechanical behaviour of the disc. During mechanical loading fluid is actively pressed out of the nucleus, combined with a rapid stretching of the annulus fibres, while during recovery fluid flows back slowly due to osmotic differences.

Prolonged mechanical loading changes the osmolarity of the intervertebral disc. The instantaneous water content of the disc depends on the loading history of the disc. Therefore the mechanical properties of the intervertebral disc (e.g. disc stiffness and height) are not an intrinsic property, but change with the loading history.

In the third chapter, it was hypothesized that blood clots in the endplates were the limiting factor for inflow. In chapter 6 a study to further test this hypothesis is described. Mechanical properties of two groups of discs were compared. In one group heparin was used to prevent blood clotting in the endplates, while the endplates of the other group were untreated. It was also attempted to achieve a stationary mechanical behaviour in a protocol that mimics the ratio of loading time versus the unloading time of a diurnal loading cycle. Thus when the duration of the loading phase exceeded that of the recovery phase by a factor of two.

The intervertebral discs were tested for 24 hours, divided into 8 separate loading cycles. Each cycle consisted of a loading phase (2 hours of sinusoidal loading) and a recovery phase (1 hour, static loading). When comparing the mechanical behaviour of the treated discs with the control group no improvement in disc recovery was found. These results are in line with the outcome of the experiments in chapter 4, where no differences were found in a comparison between discs with open and closed endplates. The combined results make our previously postulated hypothesis that obstruction of the endplate is responsible for the difference between the mechanical behaviour of the loading and the unloading phase unlikely since recovery appeared to be slow in all cases.

The overall mechanical behaviour of both groups stabilized after three cycles. From then on the recovery phase compensated the changes of the loading phase. This implies that fluid flow out of the disc can be compensated during recovery, even when inflow in general is slower than outflow. However, since fluid flow is a slow process it is unlikely that a full recovery of water content in the nucleus was reached. Visco-elastic behaviour dominated the overall mechanical behaviour of the disc from the third cycle. The results show that a dynamic equilibrium, similar to the *in vivo* situation, can be reached *in vitro*. However, if a full exchange of fluid of the nucleus with the environment is required, a long recovery phase (minimum of eight hours) should be part of the test.

Mechanical loading on the intervertebral disc leads to loss of disc height both *in vivo* and *in vitro*. The *in vitro* results presented in this thesis can be translated to the in vivo behaviour of human discs. Change of disc height is caused by a combination of a change in water content and elongation of annulus fibres. The large difference in time constants between adaptation to an increased mechanical load and a decreased mechanical load suggests that two different processes are responsible. During axial compression the increased hydrostatic pressure squeezes fluid out of the disc, while during unloading the changes in osmotic pressure drive fluid back into the disc. The latter is a slow process. Therefore the cyclic behaviour during daytime is mainly visco-elastic; the nucleus fluid acquired during night is already lost during the first hour after rising.

In vivo the disc is never without loading. The loading history of the intervertebral disc determines the instantaneous mechanical properties of the disc. The disc height and the stiffness vary with the water content of the nucleus in a daily cycle. High compression loads of every-day activities *in vivo* are known to be responsible for damage to the endplates. Several studies link endplate damage to degeneration. Disc properties shortly after rising presumably differ from the properties during daytime. Avoiding high external loading shortly after rising in the morning when the disc is super-hydrated might reduce the risk of endplate fracture and herniated discs.

These results also have implications for testing of motion sections and intervertebral discs. The motion segment is a complex, time- and load-dependent system; during sustained loading each part plays a distinct role in the mechanical behaviour of a segment in time. Specimens for mechanical testing should therefore be tested as complete as possible: both endplates and only half of the supporting trabecular bone of vertebral body present, thus the outer endplates removed.

Since mechanical properties of motion segments and discs shortly after rising differ from the properties during daytime, a mechanical test should be designed for the desired time point in the daily cycle. Therefore, preloading of the specimen is required.

Finally, results of studies on disc properties like disc height, creep rate and stiffness can only be mutually compared with other studies when the tested discs have the same loading history. Again preloading of the disc is required to bring the disc in this required state.