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The use of a quadruped as an in vivo model for the study of the spine – biomechanical considerations

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Abstract Animal models in spine research are often criticized for being irrelevant to the human situation due to the horizontal position of the spine. Whether this is justified from a biomechanical point of view can be questioned. The purpose of the study reported here was to provide arguments that a quadruped can be a valuable in vivo model for the study of the spine in spite of its horizontal position. Relevant literature is reviewed, and biomechanical analyses were made of the standing and walking quadruped. Further, the vertebral trabecular bone architecture was quantitatively analysed by computer and interpreted in the light of Wolff's law. Due to the fact that spinal segments cannot withstand substantial bending moments, additional tensile forces from muscles and ligaments are necessary to control the posture of a quadruped spine. As a consequence, the spine is mainly loaded by axial compression. The trabeculae in a goat's vertebral body were found to course horizontally between its anterior and posterior endplates, implying that the main load within the vertebral body was indeed an axial compression force. The density of the vertebrae of quadrupeds is higher than that of human vertebrae, suggesting that the quadruped has to sustain higher axial compression stresses. The quadruped spine is mainly loaded along its long axis, just like the human spine. The quadruped can thus be a valuable animal model for spine research. An important point of difference is the higher axial compression stress in quadrupeds, which leads to higher bone densities in the vertebrae. This puts some limitations on the transferability of the results of animal experiments to the human situation.

Keywords Quadruped · Animal model · Spine · Mechanical load · Trabecular bone architecture

Introduction

A wide variety of implants and procedures are available to the surgeon for the treatment of spinal deformities. Generally, the goal of a surgical intervention is to correct or prevent spinal deformity, to stabilize the spine after fracture or osteotomy, and/or to eliminate painful movements between vertebrae. Spinal instrumentation thus primarily has a mechanical function. Therefore, many biomechanical studies have been performed in order to optimize size, shape and material of implants.

In order to mimic the clinical situation as much as possible, spinal implants have often been tested in vitro on human cadaver segments [6, 17, 20]. One problem with the use of human specimens, however, is the large variation in geometry and mechanical properties. Another problem is the difficulty in obtaining human specimens, especially from the younger population. Therefore, most in vitro experiments have been performed in animal spines (see, for example, references 1, 2, 13, 34], which are more easily available and have more uniform geometrical and mechanical properties. As for clinical relevance, their similarity with human spines from the anatomical and mechanical points of view has been well described [8, 38, 41, 42].

Thus implants mechanically stabilize the spine directly after the operation. Usually, however, the ultimate goal of the operation is to obtain a bony bridge between adjacent vertebrae. This fusion process not only depends on the loads and motion within the bridged segment, but also on biological aspects such as growth factors, blood supply and biocompatibility of the materials used. In vivo animal models are thus indispensable in the study of the process of spinal fusion [7, 21, 29, 35, 36, 39]. At the same time, however, the relevance of animal models to human spine research has been questioned [4, 10, 11, 15, 26, 45], and indeed there would appear to be some justification for this view since dogs, sheep and goats are quadrupeds, and their spines supposedly are subjected to loads that differ considerably from those in humans.

It is generally widely accepted that quadruped spines are subjected to loads different from those in the upright human spine [4, 10, 11, 15, 26, 45]. It must be emphasized, however, that this opinion is not substantiated in the literature: neither experimental nor theoretical studies were found that show a fundamental difference between the mechanical loading of quadruped and biped spines. On the contrary, several studies show striking similarities in geometry [8, 18, 43], indicating that quadruped and biped spines must be loaded in a similar way. This idea is further substantiated by studies in which the mechanical properties of spinal segments of sheep, calf and humans have been shown to be comparable [41, 42]. One finite element study has shown that the stress distributions in canine and human motion segments under physiological loads are similar, thus strengthening the justification for the use of quadruped in vivo models for the study of the spine [19].

The biological aspects of the use of animal models for spine research have been reviewed by Schimandle and Boden [29]. In the present report the use of a quadruped as an in vivo model is discussed from the biomechanical point of view. Biomechanical analyses are presented of the standing and walking quadruped. An analysis of the vertebral trabecular bone architecture is also presented. Emphasis is laid on differences between quadruped and human spines and their consequences for the interpretation of results obtained with in vivo animal models.

Spinal loads in a standing quadruped

From the mechanical point of view, a quadruped is a complex system. There are different types of joints, and the distribution of the muscles and their activity during movements are largely unknown. In fact, the redundancy of the muscular system makes it impossible to determine the actual loads in a living system. Nevertheless, mechanical principles also apply to animate systems, and some conclusions can be drawn from a global study of the statics of a vertebrate as a whole.

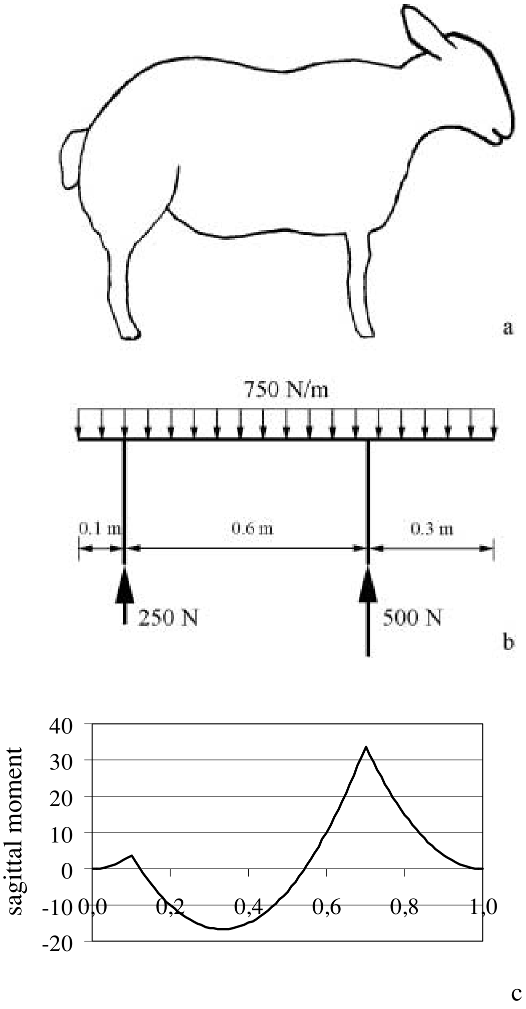

Fig. 1 Bending moments working on an idealized sheep due to gravitational force. Positive moments tend to flex, negative moments tend to extend the spine. Note that the sagittal moments are large compared to the flexion/extension stiffness of a spinal segment [42]

First, consider a sheep of 75 kg standing symmetrically on its four feet (Fig. 1a). Assume for the sake of simplicity that the weight is evenly distributed over its body with a length of 1 m. Then the front feet carry 500 N, and the hind feet 250 N (Fig. 1b). Also the moments working on the spine due to gravity can be calculated (Fig. 1c). These are rough but low estimates because in reality the body mass is more concentrated in the head and in the stomach. The point is that considerable bending moments act on the spine in the sagittal plane, even in normal standing.

With this in mind, it is important to note that a spinal segment may well resist axial compression, ventral and lateral shear, and – at the lumbar level – torsion [31, 32, 40, 41, 42]. However, in any case of bending, only ex-

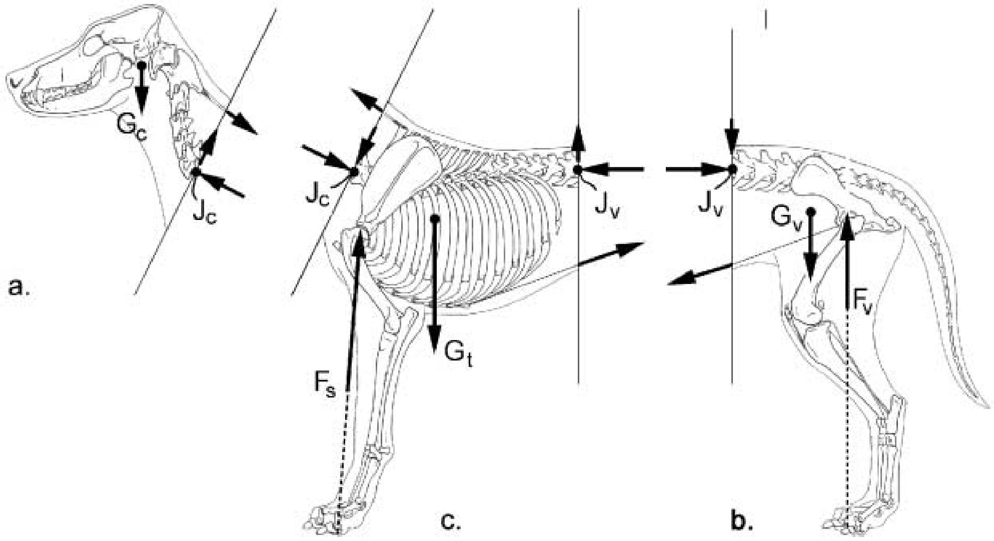

Fig. 2 Free body diagrams showing the equilibrium of forces and moments in the cervical, the thoracic and the lumbar spine in a dog. *a* The weight of head and neck (G_c) introduces a flexing moment around cervical joint J_c. To prevent this part from sagging, a tensile force T_c is required, which is mainly provided by a passive structure called the funiculus nuchae. The musculi splenius and scaleni (not drawn) provide additional stability and allow extension and flexion of the cervical spine, respectively. Equilibrium of forces is maintained by a compressive force on the vertebral body F_b and a facet joint force F_f. *b* The lumbar spine is loaded by a flexion moment due to pelvic force F_p and a gravitational force G_l, which is counterbalanced by a tensile force T_l and a lumbar compression force F_b in joint J_l. The resultant of F_b and facet joint force F_f is equal and opposite to the resultant of F_p, G_l and T_l. *c* The thoracic spine is loaded by a shoulder force F_s, a gravitational force G_t, tensile forces T_c and T_l, and the vertebral loads F_b and F_f in the cervical and lumbar joints J_c and J_l. As a consequence, the thoracic spine is also mainly loaded by axial compression due to the vertebral body forces F_b

treme distortions are counterbalanced by ligaments or other passive structures. This follows from the relatively low bending stiffness of spinal segments. For example, the range of motion of the thoracolumbar sheep spine under a flexion and extension moment of 7.5 Nm is some 58º and 70º, respectively [42], whereas the sagittal bending loads in normal standing are up to four times as high (Fig. 1c). Yet the sheep is well able to keep its spine in a more or less straight position. The role of the musculature can also be appreciated by the slackness of a sleeping or anaesthetized animal: without muscular activity, a spine just cannot maintain its posture.

In addition, in order to reduce the energy required to prevent sagging of the head or the trunk, passive structures are present in most quadrupeds, such as the funiculus nuchae in the neck (Fig. 2) or the linea alba in the ventral region of the trunk [24]. Together with the axial compression load in the spine, the tensile forces in these structures counterbalance the sagittal moments imposed by gravity. The spine – quadruped as well as human – can thus be regarded mechanically as a series of freely hinged vertebrae needing further support from tensile structures to control posture.

Muscles and ligaments thus play an important role in the posture of a quadruped and the loads that work on the skeleton. For example, for the head and neck of a dog to stay at rest, the condition of equilibrium is that the resultant of forces and moments is zero (Fig. 2). As spine segments do not resist substantial bending moments themselves, equilibrium must be provided by forces from dorsal muscles or ligaments. Consequently, the spine itself is mainly loaded under axial compression, despite its far from vertical position. In fact, the cervical spine works like a crane, with struts that are only loaded by tension (the muscles and the funiculus nuchae) or compression (the vertebrae). Thompson [37] pointed out that animals with heavy heads or long necks are able to exercise high counterbalancing moments because they have long thoracic spinous processes which provide a long moment arm for the extending forces.

A similar analysis can be performed for the thoracolumbar spine. The part of the trunk with a negative moment (Fig. 1b) has the tendency to extend due to gravitational forces. In effect, the ventral part of the trunk is stretched under its own weight, while the dorsal part is compressed. This compressive force is resisted by the spine, while stretching is cushioned by the ventral muscles, particularly effectively by the musculus rectus abdominis, which of all muscles has the longest lever arm to the spine, and the passive tensile band linea alba [24]. The free body diagram in Fig. 2b shows that the lumbar part of the spine is also mainly loaded by axial compression.

It is interesting to note that the pelvis and thorax are used as skeletal levers for flexing the spine. Three types of forces may act like this: (1) an abdominal ligamental and/or muscle force; (2) the muscular forces counterbalancing the gravitational force on the protruding parts of the trunk (head and tail); and (3) forces from the extrinsic leg muscles, such as the biceps femoris on the pelvis and the anterior pectoralis on the thorax. Other extrinsic leg muscles, such as the psoas and the latissimus dorsi, function as extensors of the spine. (For a more detailed anatomy of dogs and horses, see reference 24.) All these muscles work together to balance the trunk and the legs, which can be achieved in a large variety of ways. The whole skeletal musculature thus must be regarded as a coherent functional unit, not as a series of independent muscles.

Spinal loads in a walking and running quadruped

Even more than a standing animal, a walking quadruped is a complex mechanical system, because loads on the feet are asymmetrical with respect to the midsagittal plane, and inertial forces cannot be neglected. The details of quadruped locomotion dynamics are beyond the scope of this paper, but it must be borne in mind that the loading of the spine is mainly under control of muscles, and that the largest loads work when the animal moves.

In a quadruped walking slowly, at least one foot is off the ground during the whole walking cycle (Fig. 3) [23]. Consequently, both thorax and pelvis are loaded asymmetrically. This effect is increased for higher walking speeds, and finds its maximum in trotting, when diagonal legs swing more or less in unison [16, 24]. This is a very stable and efficient way of locomotion, because the connecting line of the supporting feet passes close under the centre of gravity. However, the spine is in maximum torsion, because pelvis and thorax are loaded by opposite torsion moments. In the gallop, in contrast, contralateral feet are more or less in unison (Fig. 4a), resulting in a more symmetrical running pattern [16]. The stride length is considerably increased by flexion and extension of the trunk, which requires free vertebrae between thorax and pelvis. Both lumbar spine anatomy and galloping are typical of mammals, and must be related to the development of this relatively new form of terrestrial locomotion [9].

During the different forms of locomotion, axial torsion, flexion-extension, and lateral bending moments are thus important loads that work on the spine. With typical pelvic forces up to 140% body weight during normal gait [3] and a lever arm of some 10 cm for axial torsion (distance from femoral head to the mid-sagittal plane of the spine), the axial torsion moment may reach a peak value in the order of 100 Nm in sheep. Similar estimations can be made for flexion-extension and for lateral bending. Obviously, such moments would severely deform the thoracolumbar spine if it were to resist these loads on its own. However, Schendel et al. have shown in an in vivo study in dogs that the deformations of the vertebral segment at the L2-L3 level are limited to 1.3º, 1.8º and 4.25º in axial torsion, extension, and lateral bending, respectively [28]. This means that tensile structures such as muscles and ligaments must be active to compensate for the applied moments, leaving the spine under considerable axial compression.

In the case of axial torsion, it is important to differentiate between lumbar segments and the higher thoracic lev-

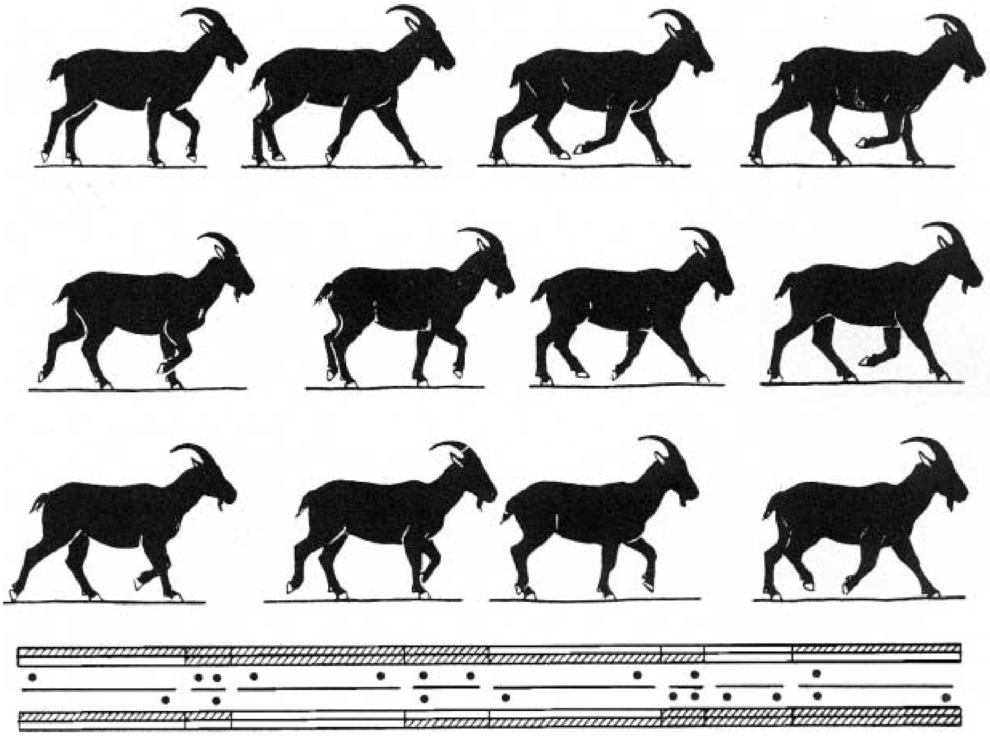

Fig. 3 Normal walking pattern of a goat and its support graph showing periods of ipsilateral and diagonal support of the trunk (after Muybridge [23])

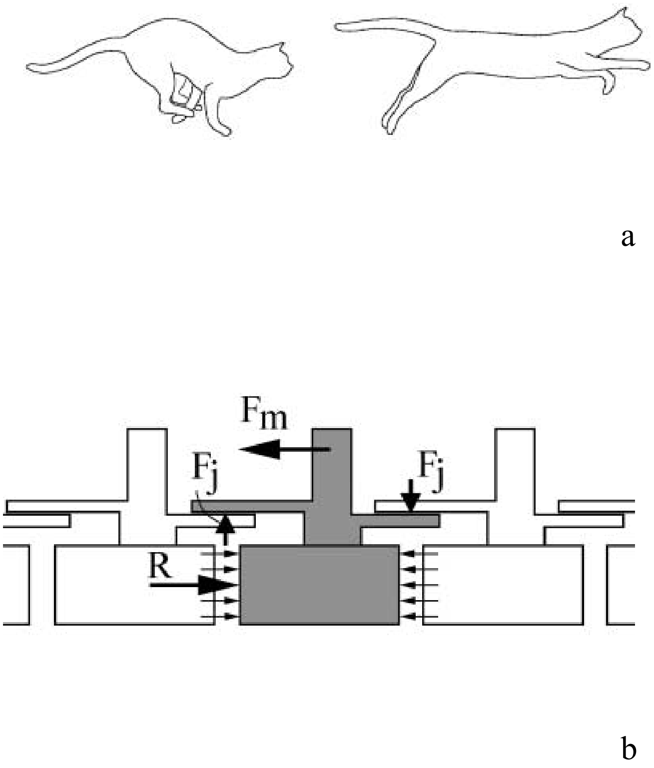

Fig. 4 **a** Extension of the spine in a cat during high speed running. **b** Forces on a vertebra during such an extension of the spine. The divided loads on the endplates represent normal axial compression. When a muscular force F_m acts due to the musculi erectores spinae, the caudal force is balanced by a reaction force R on the endplate, which thus is loaded by increased axial compression. The couple introduced by F_m and R is counterbalanced by the facetal joint loads F_j. The array of facet joints thus forms a lever arm for the dorsal muscles that extend the spine. White and Panjabi [40] pointed out that the pedicles are most resistant to this type of loading

els. The more caudal parts of the spine are quite stiff (3.3–7.1 Nm/degree), and well able to transfer torsional loads to the pelvis under small segmental rotations [31, 32, 42]. This is due to the position of the facet joints, which are oriented at an angle between the sagittal and frontal planes [8, 40]. In the thoracic segments, however, the facet joints are more or less aligned in the frontal plane, which leads to a much lower stiffness (1.0–2.1 Nm/degree), allowing larger rotations [40, 43]. Again, muscular forces or ligaments are required to prevent major distortions of the upper trunk. Good candidates for this function are the oblique abdominal muscles. As in the case of sagittal bending, the thoracic ribcage functions as a lever arm for these compensating forces, and the axial component of these muscular forces puts the spine under axial compression. It is interesting to note, that the torsional stiffness of the quadruped spine is similar to that of the human spine [41, 42], indicating that in both cases the lumbar spine may be loaded under torsion, but that at the thoracic levels the torsional moment must be compensated by muscular forces.

A special case of spinal loading is the gallop. It is essential that the propulsive force is generated by the hind legs, and that the trunk is actively extended in order to increase stride length (Fig. 4a). The muscular forces are mainly generated by the biceps femoralis in the legs, and the musculi longissimus and multifidus along the dorsal spine. Every single vertebra is thus loaded by an explosive, extending force. The intervertebral disc is not quite able to resist this moment [31]. However, the array of facet joints that lie above each other like tiles in a roof construction, forms a lever arm for the erectores and prevents the spine from overstretching (Fig. 4b). The facet joints thus play an important role in jumping and running. From Fig. 4b it can be appreciated that the vertebral bodies are mainly loaded by axial compression, whereas the pedicle joints are mainly loaded under sagittal bending [31, 32].

During standing and walking, quadruped spines may thus be subjected to all kinds of loads. However, as the vertebral column hardly resists bending moments, muscles are necessary to control posture and movements, which leads to additional axial compression of the spine. In the case of torsion, the same applies to the thoracic levels, but at the low thoracic and lumbar level, the facet joints play an important role in transferring axial torsion moments to the pelvis [28]. It is interesting to note that this also applies to the human spine in which rotation at the lumbar level during walking is minimal [12]. The quadruped spine thus appears to be loaded in a very similar way to the human spine.

The trabecular bone architecture in a quadruped vertebra

The quadruped spine is thus mainly loaded by axial compression, and other basic loads are transformed by the appropriate musculature into axial compression and, eventually, facet joint loads. It is also known that the architecture of bone is closely related to its mechanical function. As postulated by Meyer [22] and Wolff [44], bone is arranged in such a way as to optimally bear the physiological loads, an observation often referred to as Wolff’s law. Although this “law“ also applies to cortical bone, it shows most clearly in trabecular bone in which struts and plates are aligned along the “lines of principal stress” or trajectories. The theory is that these trajectorial structures arise from the process of functional adaptation during which unloaded bone gets resorbed and mechanical stimulation induces bone formation [27]. Generally, the ability of bone to adapt to mechanical loads provides each vertebrate with a bone architecture that optimally suits its individual needs. It is interesting to consider that bone adapts to heavy loads rather than to minor loads, and only to regular loads of daily life. Locomotion thus is a strong me-

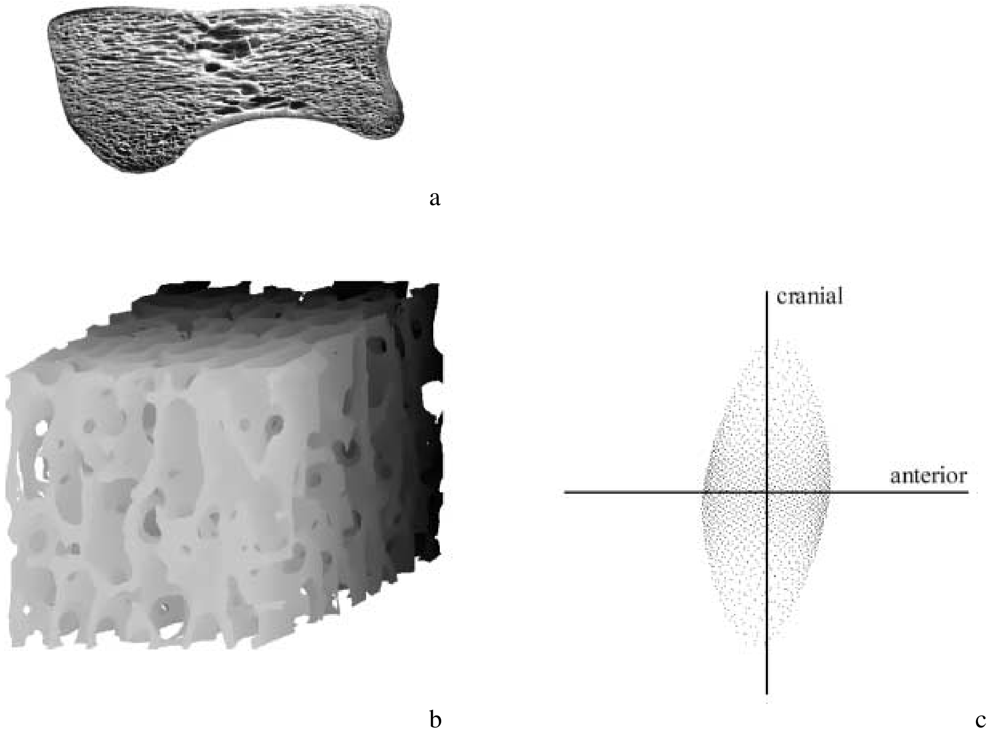

Fig. 5a–c Trabecular bone structure in a goat vertebra. **a** Sagittal section showing trabeculae running from endplate to endplate. **b** Three-dimensional computer reconstruction of a bone cube near the endplate (8 mm). Bone density is 26%, about twice as high as in humans [31]. **c** Star Length Distribution [33] (SLD) of the same specimen. Anisotropy of the specimen is 2.7, which is a strong vertical orientation. For comparison, young human vertebrae typically show anisotropies in the range 1.3–2.2 [31, 32]

chanical stimulator of bone tissue, whereas incidental high speed running and high impact loads are not.

The vertebral trabecular bone architecture thus provides information on how the vertebral body is loaded. In the case of the human spine, this has been studied in quite some detail [30, 31, 32]. The human spine is mainly loaded by axial compression, resulting in a bone architecture oriented from endplate to endplate. From the analyses in the previous sections, we thus should expect a similar trabecular bone architecture in a quadruped vertebra. Figure 5a shows that this is indeed the case, strongly supporting – if not providing evidence for – the theory that the quadruped spine is also loaded mainly by axial compression. The anisotropy of the trabecular bone architecture can be quantified by the Star Length Distribution (SLD) [33], which appears to be higher in the goat vertebra than in the human vertebra (Fig. 5c). Trabecular bone in the goat spine is also denser by a factor of two, indicating that the axial compression stress in quadrupeds may be even higher, despite their horizontal position.

Discussion

The purpose of this study was to determine whether a quadruped could be a valuable in vivo model for the study of the spine. An analysis of the standing and walking quadruped showed that considerable bending and torsion moments must be sustained by the horizontal trunk. Due to the low resistance of the spine against such loads, these moments must be counterbalanced by tensile forces from muscles and/or ligaments and a compression force in the spine. Further, the vertebral bone architecture was analysed to show that trabeculae run from endplate to endplate, indicating that the main load in the quadruped spine is indeed axial compression. Together these analyses suggest that the use of a quadruped as an in vivo model for spine research is justified, at least as far as the loading conditions are concerned.

In this context, it is interesting to consider the concept of a follower load, introduced recently by Patwardhan et al. [25]. In an elegant experimental set-up, they showed that the load-carrying capacity of a curved lumbar spine increases dramatically if the compressive load follows the curvature of the spine. The application of such a load can only be realized by internal, i.e. muscular and ligamental, loads, and seems to function optimally if the load path remains within a small range around the centres of rotation of the lumbar segments. In other words, the spine, consisting of “hinged” vertebral bodies with limited bending stiffness, is stabilized best within the neutral zones of the individual segments by a load that follows its curvature. It also follows from this concept that the curvature of the spine does not influence the way a spinal segment or an intervertebral disc is loaded.

It is also important to point out the differences between human and quadruped spines because these may have consequences for the interpretation of experimental results. Most important is the density of the trabecular bone structure. That animals have higher vertebral bone densities is a strong indication that axial compression stress is higher than in humans. This has in fact been confirmed by a recent in vivo study [14]. As a consequence, quadruped vertebrae are stronger than human vertebrae. For example, lumbar goat vertebrae with a cross-sectional area of some 25%, are approximately as strong as lumbar vertebrae of humans [34]. This fits well with the finding that bone density differs by a factor two (Fig. 5), because bone strength increases with the second power of density [5]. If then an intervertebral cage or a pedicle screw is inserted in a quadruped, the implant obviously has a stronger mechanical hold than would be the case in human vertebrae. This also means that bone in, for example, a fusion zone between two vertebrae may be subjected to stronger mechanical stimuli to form bone. This could explain why dog models show solid fusions in almost all animals, unlike the clinical situation in humans [29]. Also, subsidence of a cage into the vertebral body may be underestimated when used in a dog or a goat [39]. Therefore, one should be careful in transferring results from quadrupeds to the human situation.

Another difference is the position of the lumbar facet joints. In humans, articular surfaces have an angle of more than 60º to the frontal plane, while in quadrupeds it is less than 30º [8]. Probably, this is related to the forces occurring in bipedal locomotion. Humans, for example, always walk asymmetrically, whereas quadrupeds have their strongest facetal loads during symmetrical gallop. Nonetheless, the stiffness of the lumbar segments to axial torsion remains more or less the same [41, 42], which suggests that the facet joints have a similar function at least in normal walking.

It is interesting but difficult to speculate which of the commonly used animal models for the study of the spine is the best. Obviously, there are many aspects to consider when choosing an animal model [29], among them the specific question of the study and the similarity of the model to the human situation. If spinal instrumentation or disc problems are of interest, pigs are probably most useful because they most closely approximate the size and shape of the human spine. It must be realized, though, that due to the higher vertebral bone density in pigs, problems with loosening of an implant will be underestimated. On the other hand, the safety of the instrumentation in respect to strength also may be underestimated due to the higher loads in a pig spine. If the biological process of spinal fusion is of interest, smaller, skeletally mature animals may be more useful, as lower costs and faster fusion times will allow a larger number of animals to be included, thereby increasing statistical significance [29]. Due to the discrepancy between spinal load and vertebral size in quadrupeds as compared to humans, it is mandatory to include proper controls in any animal study of the spine.

Striking similarities exist between the spines of humans and quadrupeds. Considering the close evolutionary relationship between mammals, this is not very surprising from a Darwinian point of view. However, in the light of Wolff's law, this means that the quadruped spine is essentially loaded in the same way as that of a human. In this paper, arguments are given that support this notion, thereby justifying the use of a quadruped as an in vivo model for the study of the human spine. An important point of difference is that the axial compression stress in quadrupeds is higher, which leads to higher bone densities in the vertebrae. This puts some limitations on the transferability of the results of animal experiments to the human situation.

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