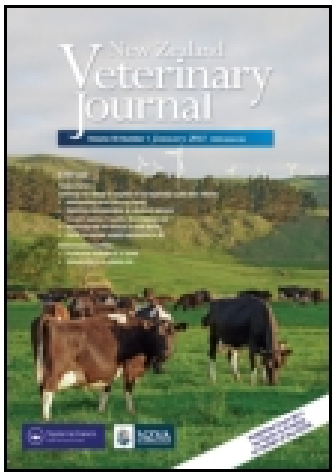

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Pathophysiology and diagnosis of third carpal bone disease in horses: A review

CJ Secombe [a b], EC Firth [a], NR Perkins [a] & BH Anderson [a c]

[a] Institute of Veterinary, Animal and Biomedical Sciences, Massey University, Palmerston North, New Zealand

[b] Division of Veterinary and Biomedical Sciences, Murdoch University, Murdoch, Western Australia E-mail:

[c] Ballarat Veterinary Practice, 1410 Sturt St, Ballarat, VIC 3350, Australia

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Review

Pathophysiology and diagnosis of third carpal bone disease in horses: a review

CJ Secombe*§, EC Firth*, NR Perkins* and BH Anderson*†

Abstract

Third carpal bone (C3) disease is a significant cause of lameness in Standardbred and Thoroughbred horses. The bone density of C3 increases as a result of exercise, reducing the compliance of the bone and predisposing it to injury. Currently, the most widely used method of diagnosis is subjective radiography using the tangential view. Radiographically, increases in bone mineral density (BMD) appear as sclerosis but it is not known at what point increases in sclerosis indicate the onset of disease or increased risk of C3 fracture. A quantitative assessment of the BMD of C3 in horses would improve understanding of the changes that occur within this bone and guide athletic management, as it is thought that BMD changes precede articular cartilage damage.

Methods of non-invasive bone-mineral analysis used for the detection of osteoporosis in humans include single photon absorptiometry (SPA), dual x-ray absorptiometry (DXA), computed tomography (CT), radioabsorptiometry (RA), quantitative ultrasonography (QU) and magnetic resonance imaging (MRI). To date, DXA and RA are the most commonly used methods of quantitative non-invasive bone-mineral analysis in horses. The cost of equipment and difficulties in performing DXA in live animals preclude the routine use of this technique for diagnostic purposes. RA may become clinically applicable to C3 analysis in horses, but small variations in x-ray beam angle when taking the tangential view significantly affect results, making this technique clinically inapplicable at this time. Currently, methods of quantitative non-invasive bone-mineral analysis of C3 in horses are not suited to clinical application.

KEY WORDS: *Horse, lameness, carpal bone, bone-mineral analysis, absorptiometry, computed tomography, quantitative ultrasonography, magnetic resonance imaging.*

Introduction

Retrospective studies performed in several countries have demonstrated that lameness appears to be the most common resaon for disruption of training schedules of performance horses, resulting in lost days in work, a prolonged spell, or retirement from racing (Jeffcott et al 1982; Rossdale et al 1985; Lindner et al 1992). The carpus is a common location of disease causing lameness. Fractures of the carpal bones during training or racing may account for 1–8% of all injuries in some populations (Mohammed et al 1991; Wilson et al 1992; Mizuno 1996). C3 is one of the more commonly injured carpal bones, (Schneider et al 1988), the frequency of injury being higher in Standardbred horses than in Thoroughbreds (Park et al 1970; Palmer 1986; McIlwraith 1996; Mizuno 1996; Lucas et al 1999).

Increased bone density or sclerosis of C3 may be the earliest indicator of disease within this bone and slab fractures are likely to be the end result of disease (Pool 1996). Subchondral lucency and cartilage lesions of the radial and intermediate facet of C3 have recently been described as a separate clinical entity and may involve the same pathophysiological process, and perhaps precede slab fractures (Ross et al 1989; Moore and Schneider, 1995).

Scientific knowledge regarding the diagnosis, treatment and prognosis of osseous disease has increased greatly over the last 30 years. Research aimed at preventing osseous disease has received less attention, the exception being the development of a variety of non-invasive methods of bone-mineral analysis used in the prevention of osteoporosis in humans. Such methods may be useful for the detection of changes in the skeleton of horses trained for athletic pursuits. However, all of these techniques have been developed to detect a decrease in bone mass, rather than an increase in bone mass such as occurs with C3 disease in racing horses. This paper reviews the pathogenesis and diagnosis of C3 disease, the current methods of non-invasive bone-mineral analysis and their application to the horse.

Pathophysiology of C3 Disease

In most horses, the carpus consists of 7 carpal bones arranged in 2 rows between the radius and the metacarpal bones. C3 is the largest bone of the distal row, contributing to two-thirds of the

* Institute of Veterinary, Animal and Biomedical Sciences, Massey University, Palmerston North New Zealand.

† Current address: Ballarat Veterinary Practice, 1410 Sturt St, Ballarat VIC 3350, Australia.

§ Author for correspondence. Current address: Division of Veterinary and Biomedical Sciences, Murdoch University, Murdoch, Western Australia. Email: csecombe@central.murdoch.edu.au

BMC	Bone mineral content
BMD	Bone mineral density
C2	Second carpal bone
C3	Third carpal bone
C4	Fourth carpal bone
CT	Computed tomography
DXA	Dual x-ray absorptiometry
MRI	Magnetic resonance imaging
QU	Quantitative ultrasonography
RA	Radiographic absorptiometry
SPA	Single photon absorptiometry

medial to lateral dimension. The 2 facets of the proximal surface are separated by a dorsopalmar ridge. The medial facet (concave), known as the radial facet, articulates with the distal surface of the radial carpal bone. The lateral facet (concave dorsally and convex palmarly) is known as the intermediate facet and articulates with the distal surface of intermediate carpal bone. The distal surface of C3 articulates almost entirely with the third metacarpal bone, and the lateral and medial aspects of the bone articulate with the fourth metacarpal bone and second metacarpal bone, respectively (Getty 1975).

When axially loaded during maximal exercise, most of the carpal articulations allow an interlocking wedge arrangement to be formed. Some of the load is transferred to the intercarpal ligaments (Bramlage et al 1988). It is thought that through this mechanism, sudden stress is converted into a longer elastic loading stress and thus the strain rate is decreased (Deane and Davies 1995). It appears that the carpus requires such a mechanism for energy absorption as its elastic ability to over-extend is limited by the palmar soft tissues when supra-physiologic loads are applied. This dispersal of energy may not occur on the medial aspect of the intercarpal joint, as loads from the radius may pass on to the radial carpal bone and directly on to the radial facet of C3 without being dissipated to the intercarpal ligaments. This predisposes the 3 major weight bearing bones to injury, in particular the radial facet of C3 (Bramlage et al 1988).

When the major weight-bearing carpal bones are loaded, the fluid component of the articular cartilage exits causing instant deformation. As the load is shifted to the solid component of the articular cartilage there is slower 'creep' deformation, which continues until equilibrium is reached between the cartilage and the external force applied; this is typical of all viscoelastic materials (Palmer and Bertone 1996). Collagen is concentrated in the superficial zones of articular cartilage, providing tensile strength. Consequently, small pathological alterations within this area may weaken the articular surface and its resistance to shear, tensile and compressive forces (Setton et al 1993). Compliant subchondral bone acts as a shock absorber between articular cartilage and epiphyseal bone, thereby helping to minimise pathology at the articular surface. Calcified cartilage, with its intermediate mechanical properties, acts as an interface between articular cartilage and subchondral bone to reduce shear stresses (Palmer and Bertone 1996). Calcified cartilage undergoes remodelling throughout life and the processes of physiological aging and injury produce reduplication of the 'tidemark' (the junction between calcified and non-calcified cartilage), resulting in cartilage thinning (Bullough 1981; Burr and Schaflet 1997).

Bone is a constantly adapting tissue and it is widely accepted that relative density increases with exercise (Young et al 1989; Young et al 1991; Palmer et al, 1994). During exercise the subchondral bone deforms when placed under a mechanical load. Repetitive loading stimulates the osteoblasts lining the spongiosa to up-regulate, leading to thickening of the trabeculae at the expense of the intra-trabecular spaces; this is termed modelling (Pool 1996). As subchondral bone density increases the shock-absorptive capacity decreases.

In order to explain the exercise induced distribution of changes that occur within C3, it is important to study loading patterns at rest and at varying gaits. At rest the palmar aspect of both the radial and intermediate facets bear the most weight. Application of high loads in this position result in intermittent weight bearing on the dorsal aspect of both facets. When moving at slow gaits such as walking and trotting, the load is distributed evenly over the radial and intermediate facets, excluding the most dorsal aspect. Under load conditions that mimic those of galloping, the load is transferred to include the dorsal rim of the intermediate and radial facets shifting towards the dorsomedial aspect of the radial facet (Firth and Hartman 1983; Palmer et al 1994). Microradiographic examination of C3's from horses that have undergone different levels of exercise show evidence of modelling, which is particularly apparent in racing horses. When horses are actively training and racing, modelling can result in increased trabecular thickening to the point that the intra-trabecular spaces are completely replaced with bone (Young et al 1989; Young et al 1991). In a transverse section of C3, 3mm from the dorsal margin, modelling is seen as an increase in photodensity and change in bony architecture. Increased radiographic photodensity is due to increased BMD (Uhlhorn et al 1998; Cantley et al 1999; Firth et al 1999a; Firth et al 1999b). In one of these studies, Firth et al (1999a) took sagittal sections in a dorsopalmar direction of the intermediate and radial facets of C3, and radiographs were taken of the sagittal sections and compared with BMD measurements performed using DXA. In another study, Uhlhorn et al (1998) radiographed isolated C3's in a proximal–distal view and compared them with bone volume measurements obtained using morphometry. In both studies it was found that bone density in the dorsal proximal, dorsal central and dorsal distal regions of C3 was significantly greater in trained compared with untrained horses, the dorsal central regions of interest having the greatest increase in density. Similar findings have been observed in Thoroughbred horses trained on a treadmill. BMD increases in the distal dorsal region of C3, then the proximal dorsal region and finally the central dorsal region (EC Firth, unpublished data).

Bony adaptation to exercise is a physiological process. However, continued modelling in response to high loads leads to pathological changes as seen in microradiographs (Young et al 1989). Continued modelling causes sharp gradients in bony stiffness 5–10mm from the dorsal edge of C3 which may result in incomplete dissipation of forces within articular cartilage during loading, predisposing it to injury (Young et al 1991). Repetitive micro-trauma to the articular cartilage leads to chondrocyte injury, which in turn responds by producing enzymes that destroy the extracellular cartilage matrix. The gross articular cartilage changes that may be seen include yellowish discolouration, dullness and fibrillation, as well as eburnation of subchondral bone. Microscopic changes include disruption of the various zones of articular cartilage, changed chondrocyte morphology, exposure of the calcified cartilage and polishing of the exposed subchondral bone (Pool 1996). Uhlhorn et al (1998) found that bones with cartilage lesions of the radial facet of C3 had a significantly higher bone volume density than those that did not. Pool (1996) found that, although there did not appear to be a good correlation between the extent of deterioration of the articular cartilage and subchondral bone, sclerosis appeared in varying amounts in affected bones.

Remodelling occurs concurrently with modelling. True remodelling occurs when there is no net increase in BMD; repair and damage occur at the same rate. When the rate of damage (presumably from the sharp change in stiffness gradient within the subchondral bone as a result of modelling) exceeds that of repair it is presumed that microfractures disrupt the canalicular system and possibly the capillary bed. The result is a wedge-shaped

portion of ischaemic sclerotic subchondral bone within C3. This secondary lesion usually measures 8–10mm in length, 3–5mm in width and 1–2mm in depth. It is located 2–4mm from the dorsal proximal margin of the radial facet and is composed of acellular fragments of sclerotic bone, the deep surface being separated from viable compacted bone by a line of resorption. A vascular response arises adjacent to the bone to fill the trough with osteogenic granulation tissue that replaces the necrotic subchondral bone (Pool 1996).

It is suggested these lesions predispose to partial or complete slab fractures. Small areas of diseased bone appear to undergo repair without destabilisation of overlying cartilage. Unsupported articular cartilage either collapses into the underlying cavity or becomes detached. Studies of slab fractures by Pool suggest these fractures occur in pathological bone (Pool 1996). All lesions began at the dorsoproximal surface of C3 in an area of chronic injury and repair. The fracture line extends distally where it either turns obliquely to create a partial slab fracture or continues to create a compete slab fracture. Usually the proximal quarter of the fracture line appears irregular and contains fibrous tissue, the distal three-quarters appears as an acute fracture (Pool 1996).

In an attempt to adapt to the mechanical stresses of exercise, C3 subchondral bone increases in density and modifies its architecture. This physiological process becomes pathological when damage to the bone exceeds repair. In vivo and in vitro studies have demonstrated that traumatic loading induces subchondral bone sclerosis and damage to calcified cartilage before inducing damage to articular cartilage (Silyn-Roberts et al 1990; Verner et al 1992). Therefore, it has been proposed that early detection of increased BMD may be helpful in predicting degenerative joint disease and fractures (DeHaan et al 1987). Currently the most commonly used method to detect increased BMD in C3 is subjective radiography.

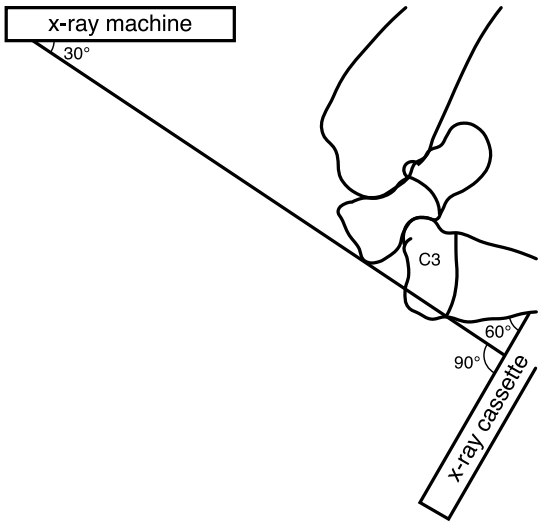

Figure 1. Tangential view of C3. The plate is angled so that the X-ray beam contacts the plate at as close to 90° as possible.

Current Method of Diagnosis of C3 Disease

Radiography is the main diagnostic tool used in the assessment of carpal injuries in horses. As with all radiographic evaluations, several views are taken to ensure adequate assessment, as superimposition is a problem in the radiographic evaluation of joints. The tangential or skyline view of the distal row of carpal bones is essential to diagnose changes in C3. There are 2 tangential views used to assess the distal carpal row. One view involves placing the plate distal to the flexed carpus and angling it towards the beam as close to 90° as possible (Figure 1). This view results in little distortion of C3, although some magnification does occur (Figure 2). The second view involves flexing the carpus and placing the plate on the dorsal aspect of the third metacarpal bone; this view causes little magnification but a significant amount of distortion, as the beam angle is not perpendicular to the plate (Figure 3 and 4). The x-ray beam angle, leg angle and C3 beam angle are similar between both views, however, the plate angle differs.

The occurrence of C3 sclerosis (an increase in radio-opacity and loss of trabecular structure) in the absence of other radiographic changes has led to the development of 2 similar grading scales used to assess this (O'Brien et al 1986; Uhlhorn and Carlsten 1999). The radiographic view used to assess sclerosis has historically been the view in which the x-ray beam angle is not at 90° to the x-ray plate (Figure 3). The radiographic quality must be such that the trabecular pattern can be recognised, not only in C3 but also in C2 and C4, as the latter is used as a control in one grading system. In the first grade, trabeculation in clearly evident, there are no areas of focal thickening and no loss of trabeculation between the cortex or medulla. In the second grade, trabeculation remains clearly evident but focal thickening is

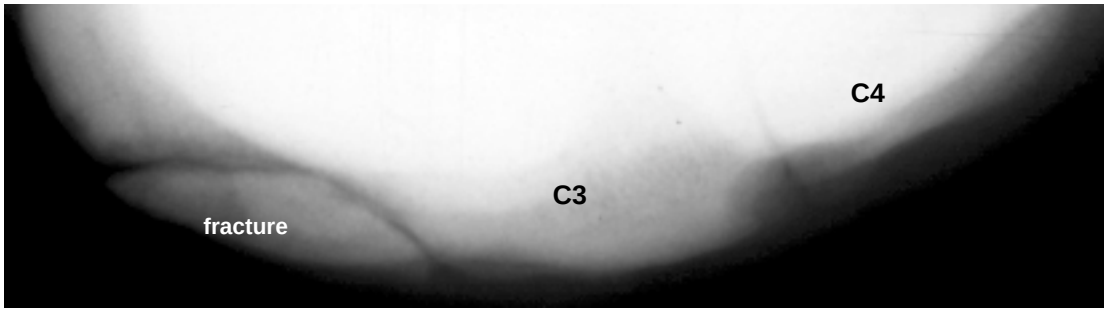

Figure 2. A radiograph of C3 and C4 using the method illustrated in Figure 1. A fracture is present within the radial facet of C3.

present. The first and second grades are believed to represent physiological adaptation (O'Brien et al 1986). In the third grade, focal loss of trabeculation and loss of definition between the cortex and the medulla occurs. In the fourth grade, the majority of the radial or intermediate facets have lost trabecular structure and definition between cortex and medulla.

C4 sclerosis is rarely seen and, if apparent, is likely to be due to radiographic artefact (O'Brien et al 1986). Investigation of subchondral bone changes within C4 have not been reported to date. There are a few reports on slab fractures of C4; these are usually sagittal fractures and are often accompanied by a slab fracture of the intermediate carpal bone. It is speculated that the cause of these fractures is abnormal force acting on normal bones, although this has not been proven (Auer et al 1986; Field and Zaruby 1994).

The subjective grading of sclerosis of C3 has been examined (Uhlhorn et al 1998). In that study, only radiographs of the tangential view in which C2 and C4 could be examined were included. Radiographs were graded, horses were euthanased and the distal row of carpal bones were disarticulated and radiographed again in a proximodistal direction. C3 was then assessed for bone volume density using bone morphometry. The authors found that subjective assessment of the tangential radiographic view allowed differentiation between sclerotic and non-sclerotic C3's, however, the grade of sclerosis could not be accurately determined. Although this is a significant finding, some degree of sclerosis is believed to be a physiological response to exercise (Firth et al 1999a), and it is currently unknown at what stage an increase in BMD and change in architecture of the subchondral bone becomes a pathological as opposed to a physiological response.

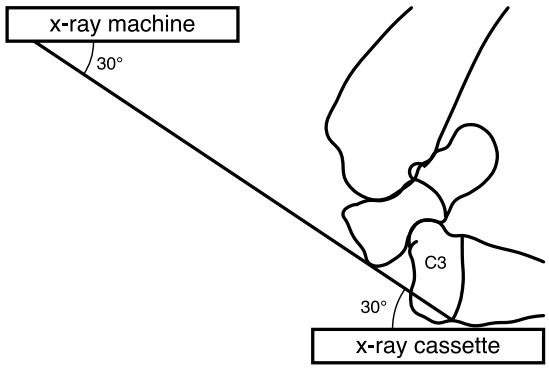

Figure 3. Tangential view of C3. The plate is parallel to the third metacarpal bone and the X-ray beam contacts the plate at 30°.

Thus, subjective radiographic analysis of changes in BMD is not without problems. It has been generally believed that changes in BMD of less than 30% cannot be detected subjectively. Although this was based on experiments performed 60 years ago (Lachmann and Whelan 1936), a more recent study agrees with this hypothesis for bones of the peripheral skeleton (Finsen and Andra 1988). Other studies have shown that, although this was true for cortical bone sites, a change of only 8–14% can be detected for bones with high trabecular content (Garton et al 1994). All of the studies reporting subjective assessments of BMD have been done in humans, in the context of detecting decreased BMD. This differs from the usual case in the young working horse in which disease is usually associated with increased BMD. As subjective analysis of radiographs may not differentiate between physiological and pathological sclerosis in C3, a quantitative method of detection of sclerosis would be useful.

Quantitative Non-Invasive Bone-Mineral Analysis – Potential Methods of Diagnosis of C3 Disease

The high prevalence of osteoporosis in humans has resulted in the development of many methods of non-invasive bone-mineral analysis in order to detect early disease and monitor its progression and response to therapy. The most commonly used methods at this time are discussed below. Non-invasive bone-mineral analysis has been used in animals, including horses, to study bone density in a number of bones.

Absorptiometry

Absorptiometry methods use the transmission of x-rays or gamma rays through the bone of interest. The degree of attenuation of the rays by the bone is measured by a scintillation detector system and there is a direct relationship between the number of photons absorbed and bone mineral content (BMC) (Mazess and Wahner 1988). As these methods do not take into account bone volume, only BMC can be measured. To assess BMD, the cross-sectional

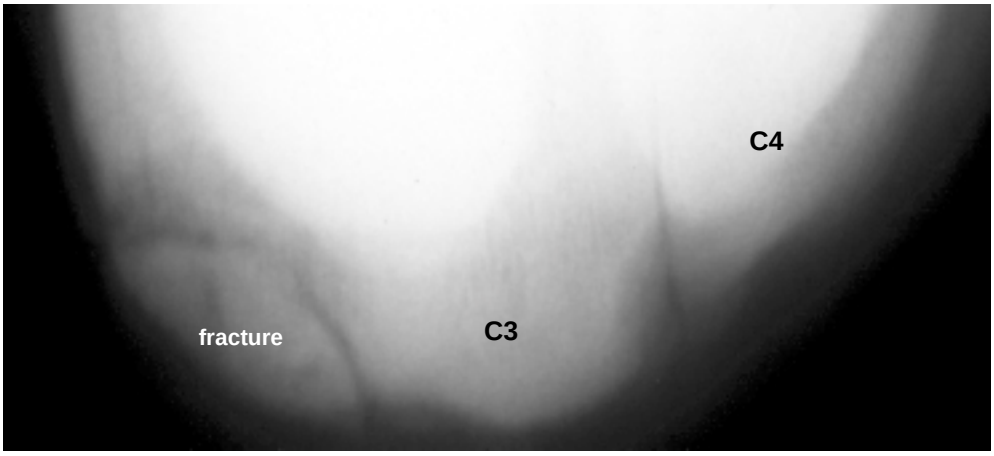

Figure 2. A radiograph of the same distal row of carpal bones as shown in Figure 2 using the method illustrated in Figure 3. A fracture is present within the radial facet of C3.

area of the bone must also be measured, for example, using ultrasonic transmission velocity; dividing BMC by cross-sectional area yields BMD (Greenfield et al 1981).

SPA, a single source of low-energy photons in the form of a radionuclide, has been used in horses to assess BMC in combination with ultrasonic transmission velocity to determine cross-sectional area, hence BMD, of the third metacarpal bone and changes that occur to BMD in response to immobilisation (Jeffcott et al 1986; Buckingham and Jeffcott 1991). Although this is a relatively precise method, it has several disadvantages, including a requirement that the horse stand still for at least 90 seconds (Jeffcott 1986). Results are expressed in terms of BMC per unit length of bone and do not take account of differences in bone size. This technique was found to only be useful for comparing changes in horses that have negligible variation in bone cross-sectional area (Jeffcott et al 1986). Although once a useful research tool, this technique is now rarely used.

DXA, developed using the principles of SPA, was introduced for commercial use in the late 1980's. The source is an x-ray tube generating x-rays of 2 distinct energy levels. These are attenuated by tissues to different degrees, eliminating the need for a constant soft-tissue covering (Mazess 1981). Numerous additional advantages over other forms of absorptiometry have made DXA the most widely used method for assessing BMD in clinical and population medicine, as well as the primary research tool for BMD assessment. In horses, DXA has only been used on excised bones (including C3), as the time taken to scan is prohibitively long for use on live subjects (Firth et al 1999a). As such, it is unlikely to have clinical application in horses for assessing BMD changes in C3.

Computed tomography

CT involves the obtainment of multiple cross-sectional images using narrow-beam x-rays and computer processing, integration and analysis of these. This method offers high levels of soft-tissue differentiation and no superimposition of overlying structures, as the third dimension is known. This results in major advantages over conventional radiography and allows the quantification of tissue densities (Hathcock and Stickle 1993). CT has recently become a popular method for assessing the BMD of trabecular bone, which has a high turnover rate compared with cortical bone, reflected by rapid subtle changes in BMD. Osseous architecture as well as BMD can be studied using this technology, resulting in a better indication of bone strength than other methods. The disadvantages of CT include exposure of patients to high doses of radiation, long scan times and, although this technique is precise and accurate, reproducibility is a problem due to inaccuracies in patient positioning (Andre and Resnick 1995; Wong and Sartoris 1996).

CT has been used in both small and large animals for the diagnosis of a variety of disorders, but little work has been done on the assessment of BMD. Detecting changes in BMD of C3 is possible using this method, but general anaesthesia is likely to be required and the high cost of equipment will limit availability.

Radioabsorptiometry

RA measures BMD objectively by measuring the radiographic photodensity of bones in comparison with that of a material of known density. The technique has been available for over 50 years but prior to the use of computers, was inaccurate, imprecise and time consuming (Yang et al 1994; Yates et al 1995). In human studies, the technique involves taking a conventional radiograph of a subject's hand together with a reference standard, both of which are placed in a predetermined position on the plate. Image analysis of the resulting radiograph is used to determine the result. The reference standard is included in the radiographic image to correct between-film differences due to film quality, exposure and processing. The ideal reference standard has the same absorption coefficient as the material being measured and the most common metallic standard used is aluminium or an aluminium alloy (Clobert and Bachtell 1981). This technique is highly accurate and reproducible (Yang et al 1994).

The consistency with which RA measures bone mass is high, even between populations and skeletal sites. RA is thought to be as good as, or in some cases better than, other bone-mass measurement techniques and its predictive association of fracture risk is high (Baran et al 1997). The technique has several advantages: it is readily available and no large capital expenditure is required. The radiographs are taken and submitted to an image analysis laboratory for interpretation, so the technique is useful in remote areas where access to other bone-mass analysis methods is limited.

RA has been used on excised dog and horse bones with limited success (Delaquerriere-Richardson et al 1982; Scotti and Jeffcott 1988). More recently, RA has been used to assess changes in BMD of the third metacarpus in live horses and found to be a useful diagnostic tool (Hoekstra et al 1999; Hoffman et al 1999). As RA has a number of advantages over other methods of BMD assessment, it may be useful in the assessment of C3 disease using a tangential radiographic view but, unfortunately, small variations in x-ray beam angle significantly affect the measured radiographic density, thereby giving false results (Secombe 2000).

Quantitative ultrasound

QU uses measurement of the speed of sound through a bone of known diameter to assess BMD. Quantitative ultrasound provides information on bone quantity and quality, as the speed of sound may be influenced by bone mass, quantities of cortical and trabecular bone and bone architecture (Grampp et al 1996; Baran et al 1997). Ultrasound beam attenuation is thought to depend on bone structure and relates to trabecular orientation and size. The more complex the structure, the more the ultrasound beam is attenuated or blocked (Baran et al 1997). There are relatively few studies assessing bone mass in women using QU, but this method has been useful for predicting fracture risk in both retrospective and prospective studies (Baran et al 1997).

Ultrasound velocity measurements have been used in horses in combination with SPA to monitor the effects of treadmill exercise on the third metacarpal bone (McCarthy and Jeffcott 1988). That study found that ultrasound velocity altered with training, but BMC and BMD did not change. This may be due to a change in the apparent architecture of the bone that was not associated with a change in BMD. To the authors' knowledge this technique has not been used to measure the BMD of C3 in horses.

Magnetic resonance imaging

MRI is commonly used clinically to assess occult traumatic or atraumatic insufficiency fractures that often occur in osteoporotic patients. MRI can detect very subtle structural changes at a fracture site and distinguish between acute and chronic defects, resulting in a high level of sensitivity and specificity when used for fracture diagnosis. Recent research suggests that MRI can be

used to determine the relationship between BMD, bone structure and strength, which is an advantage over most of the above-mentioned techniques for non-invasive bone-mineral analysis, and allows more accurate determination of fracture risk in osteoporotic patients. As the signal measured by MRI is generated by hydrogen atoms there is no radiation and therefore it can be safely used in pregnant women and children (Majumdar and Genant 1995). MRI has been used in horses, mostly on cadavers and, to the authors' knowledge, BMD and bone architecture has not been investigated in this species.

Conclusions

C3 disease is a significant problem in the equine industries, more so in Standardbred horses than in Thoroughbreds. The end stage of C3 disease is thought to be slab fractures, for which the prognosis for return to athletic function is guarded. The current understanding of the pathophysiology of this disease is that the bone adapts to exercise by increasing BMD and altering its architecture. The benefits of increased strength are to the detriment of compliance within the bone. Increased stiffness results in vulnerability to mechanical damage that cannot be adequately repaired and lesions form. It is currently unknown when physiological adaptation becomes pathological. Radiographically, increases in BMD appear as sclerosis and it is not known at what point increases in sclerosis indicates the onset of disease or increased risk of fracture.

A quantitative assessment of the BMD of C3 in horses would be useful to develop a better understanding of the changes that occur within this bone and to alter athletic management, as bone density changes are found to precede articular cartilage damage. At this point in time the only methods available are expensive, time consuming and are usually used on excised bones. DXA and RA are the most commonly used methods of quantitative non-invasive bone-mineral analysis in horses. The cost of equipment and difficulties in performing DXA in live animals preclude the routine use of this technique as a diagnostic modality. RA may become clinically applicable to C3 analysis in horses, but small variations in x-ray beam angle when taking the tangential view significantly affected results (Secombe 2000), making this technique clinically inapplicable at this time. Currently, quantitative non-invasive bone-mineral analysis of C3 in horses appears to be clinically inapplicable.

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