Key Points:

- In racehorses, fetlock lameness is commonly due to subchondral bone pain and in
  sport horses, is usually due to osteoarthritis.
- Clinical signs are often nonexistent and low palmar/plantar diagnostic analgesia
  confirms the authentic source of pain.
- Special radiographic views and advanced imaging further characterize subchondral
  bone changes and associated abnormalities.
- Treatment is challenging and although most horses return to athletic function they
  have reduced performance longevity.

In racehorses the fetlock joints, the metacarpophalangeal (MCPJ) and
metatarsophalangeal (MTPJ) joints, are the most important source of pain causing lameness and
poor performance, but clinical recognition can be perplexing, and frustrating. Subchondral bone
pain, so-called mal or non-adaptive bone remodeling, or cumulative stress-induced injury can
cause lameness without overt clinical signs underscoring the continued importance of diagnostic
analgesia to detect the authentic source of pain causing lameness. In non-racehorses the fetlock
joints are frequently a source of pain causing lameness, particularly in jumpers, dressage horses
and older horses that have developed chronic osteoarthritis (OA). There is a relationship
between chronic suspensory desmitis and OA of the fetlock joint and, there can be difficulties in
sorting out the source of pain causing lameness in horses with suspensory branch desmitis and
OA of the fetlock joint; intra-articular analgesia of the fetlock joint can abolish pain from branch
desmitis (and from oblique sesamoidean desmitis) and low-palmar/plantar (low 4-point)
algesia can abolish pain from both conditions.

Subchondral bone pain and the fetlock joint

Subchondral bone pain and lameness in racehorses and in some non-racehorses
dominates much of my clinical time. I have been interested in a clinical syndrome in both the
MTPJ and the MCPJ. The MTPJ has historically been under-recognized as a source of hindlimb
lameness but in my practice was equal in importance to the tarsus and in fact, one of the most
important sources of pain in Standardbred (STB) and Thoroughbred (TB) racehorses.1,2 In the
mid-to-late 1980’s I recognized a perplexing problem primarily in the STB MTPJ with clinical
signs consistently including decreased performance and a short-choppy gait or stride in horses
with bilateral lameness, mild to moderate lameness in horses with unilateral hindlimb lameness,
but effusion and a positive response to lower limb flexion tests were absent or inconsistent. I
now realize this syndrome is a common problem in the TB racehorse as well. Historically,
horses could be “blocked sound” but not “injected sound” according to trainers and referring
veterinarians. Low plantar perineural diagnostic analgesia was most consistent in abolishing
pain but in some horses intra-articular analgesia was effective, or partially so. Conventional
radiographs and xeroradiographs were negative or equivocal in most horses, but occasionally mild sclerosis of the subchondral bone of the third metatarsal bone (MtIII) was seen. Scintigraphy provided the answer. Focal areas of increased radiopharmaceutical uptake (IRU) in the subchondral bone of MtIII were the hallmark of this clinical syndrome.\textsuperscript{3-5} The most common area of IRU involved the distal, plantarolateral aspect of MtIII and often IRU was bilateral. IRU of the distal Mc/MtIII is the most common scintigraphic finding in racehorses with high speed lameness and/or poor performance. But, what is it?

\textit{Stress remodeling and mal or non-adaptive remodeling}

The name \textit{mal or non-adaptive bone remodeling} has been used but remodeling is a difficult concept to explain. The concept that bone changes shape and strength, modeled and remodeled, in response to the magnitude and direction of strain (Wolff's Law) explains many of the changes in bone morphology seen in the athletic horse, particularly in young racehorses. Repetitive cyclic loading of bone in racehorses causes normal, predictable change in both cortical and cancellous bone, stress remodeling, although those of cortical bone are better understood. Stress fractures of cortical (long) bones can lead to catastrophic bone failure and breakdowns. Adaptive changes in bone in response to repetitive cyclic loading include modeling, micromodeling, and remodeling.\textsuperscript{6} Modeling is the change in shape of a bone and the most familiar is dramatic change in the dorsal cortex of McIII in TBs due to the addition of normal lamellar or abnormal fiber bone in response changes in strain.\textsuperscript{6,7} Micromodeling occurs in cancellous (trabecular) bone, and is the normal process by which trabecular bone in the subchondral region strengthens and changes shape resulting from compressive and tensile forces. This process results in subchondral sclerosis and if accelerated results in deposition of biomechanically inferior woven rather than lamellar bone.\textsuperscript{6} Bone remodeling is the process by which formed bone in both regions undergoes resorption and replacement by mature lamellar bone. During resorption, bone porosity increases and stiffness decreases. When microdamage or microfracture formation outpaces bone deposition in the remodeling process, both cortical and cancellous bone are subject to fracture. In cortical bone of McIII, high strain cyclic fatigue has been proposed to cause decreased stiffness, which in turn, causes the bone to strengthen.\textsuperscript{7} Dorsal cortical fracture or stress fracture may develop if high strain cyclic fatigue occurs when the remodeling process of bone resorption is dominant.\textsuperscript{7}

In the clinical situation, the concept of a continuum of stress related bone change in both cortical and cancellous bone is useful in understanding the pathogenesis of predictable stress related bony injury that ultimately leads to the development of lameness, fractures and OA. Thus, stress remodeling, a process is sometimes referred to as adaptive bone change in the normal portion of the spectrum and mal or non-adaptive when the process becomes pathologic. It is proposed that normal bone undergoes modeling and remodeling as a response to training in order to strengthen and endure cyclic fatigue. Cortical thickening and subchondral sclerosis are normal events, but when the process becomes pathologic, sequential bone changes of stress reaction, stress fracture, and catastrophic fracture sometimes occur. Stress reaction is a term used to indicate abnormal bone remodeling which is scintigraphically, but not radiologically apparent, and is thought to precede stress fracture. Recent studies of the dorsal cortex of McIII, and in other long bones such as the tibia, humerus, and ilium, show stress related bone changes exist before fracture. Microfractures and periosteal callous indicative of stress fracture preceded
complete fracture in both the humerus and pelvis.\textsuperscript{8,9} Stress related changes of cortical bone are familiar radiographically, as thickened areas of cortex, linear areas of radiolucency corresponding to new periosteal bone formation, proliferative changes, and oblique fracture lines, representing stress fracture.

Stress related changes of cancellous bone, however, are more difficult to recognize radiologically, and diagnosis can be challenging. A remodeling scheme of distal McIII and MtIII similar to that seen in cortical bone has been proposed to account for subchondral bone changes, and later overlying cartilage damage and fracture.\textsuperscript{3,5,10} The term traumatic osteochondrosis was suggested to account for the remodeling process of distal McIII/MtIII in TBs.\textsuperscript{11} This disease has also been termed osteochondritis dissecans (OCD) of McIII, implying the problem is developmental in nature, but this term is misleading since it appears the injury is an acquired stress related lesion.\textsuperscript{12,13} While the distal aspect of McIII/MtIII remains a common region subject to stress related bone changes, the carpal bone, in particular the third carpal bone (C-3), and the distal tarsal bones are also commonly affected.\textsuperscript{12}

Subchondral bone plays a huge role in the development of joint disease, and hence I prefer to use the term OA rather than degenerative joint disease. The term OA implies there is inflammation (deterioration) of bone (osteo) and the joint (arthro). Osteoarthritis describes the overall degenerative process occurring in subchondral bone, overlying articular cartilage, and the synovial membrane and allows for the importance of the subchondral bone to be recognized. This is particularly important in young racehorses in which subchondral bone changes can be substantial. Understanding the role of subchondral bone is crucial in the diagnosis of injury, particularly early diagnosis in young racehorses, and helps to explain to clients, trainers, and colleagues, lameness without classic clinical or radiographic changes. For instance, common clinical findings of synovitis (effusion) or radiological changes such as marginal osteophytes occur late in horses with OA, yet in many of these patients, obvious scintigraphic findings and subtle radiographic changes such as sclerosis of subchondral bone or mild radiolucency will be present. It is well accepted that many of the common articular fractures, such as carpal chip fractures and McIII/MtIII condylar fractures usually occur in abnormal bone. Although fractures could be single event injuries originating from a “bad step” or “hole in the racetrack” most commonly they are the last event that occurs in abnormal bone. In summary, stress related subchondral bone changes are thought to be a normal adaptive response of cancellous bone to training. However, the process often becomes mal or non-adaptive. Ischemia (controversial) of dense subchondral bone, microtrauma or microfractures, mechanical trauma to overlying cartilage caused by dense subchondral bone, and weakened subchondral bone caused by intense resorption predispose to the development of articular fracture (such as chip or condylar fractures) or OA.

Bone scintigraphy is of tremendous value in identifying early stress related changes in bone and in monitoring healing. Focal, mild-to-intense areas of IRU in cortical or subchondral bone indicate active bone remodeling and possible fracture. Predictable sites of stress reaction or stress fracture occur in young racehorses undergoing intense race training. In cortical bone these sites such as the humerus, tibia, and pelvis are well known and accepted. In cancellous bone the common sites include the distal aspect of McIII (medial > lateral) and the distal aspect of MtIII (lateral > medial). In the continuum of events that lead from the normal adaptive response of cortical or cancellous bone to a mal or non-adaptive process (pathologic bone) and subsequent
fracture or OA abnormal scintigraphic findings often precede lameness, which in turn precedes radiographic evidence of remodeling changes or fracture. In subchondral bone, scintigraphic evidence of focal areas of IRU can help the clinician identify regions of sclerosis or radiolucency, particularly if special radiographic views are used to evaluate subchondral bone. Client communication can be difficult in young horses with stress related subchondral bone injury, simply because the classic signs of OA or fracture do not exist either clinically or radiologically. This process may be best understood by clients by referring to quotes such as “…he was making progress faster than his bones were keeping up (L Bramlage)” or simply “…he outran his bones (Searcy).”

Perineural analgesia is necessary for accurate diagnosis

I find it interesting that lameness is more likely to be abolished using perineural rather than intra-articular analgesia. This finding supports the idea that overlying cartilage damage occurs relatively late in this process and pain is emanating from subchondral bone. This could also explain the lack of clinical signs such as effusion and a positive response to flexion tests and the lack of response to intra-articular medication. Clinicians must be familiar with low palmar/low plantar (low 4-point, low volar) diagnostic analgesic techniques. I have often used a modification of this block, first proposed by Dr. Rob Pilsworth: selective analgesia of the lateral plantar metatarsal nerve for horses with the most common form of subchondral bone pain involving the distal, plantarolateral aspect of MtIII is quite effective. In the forelimb and in some horses with hindlimb lameness, both lateral and medial palmar metacarpal nerves need to be blocked. False negatives do occur and the complete low palmar/low plantar block may be necessary.

Radiography/radiology

Seeing focal areas of IRU in the distal Mc/MtIII prompted the acquisition of “down-angled” oblique radiographic views in order to adequately evaluate the condyles of Mc/MtIII for sclerotic and radiolucent changes. These views are now routinely taken and have improved our ability to evaluate the palmar/plantar aspect of the MCPJ/MTPJ; but, beware that small osteochondral fragments in the dorsal aspect of these joints can be missed on the down-angle oblique projections. On conventional horizontal oblique views the proximal sesamoid bone (PSB)s obscure the ability to evaluate the distal aspect of Mc/MtIII and in fact, in the hindlimb, there is often overlap of the distal aspect of the PSBs and the proximal aspect of the proximal phalanx. Flexed dorsopalmar/plantar views are also useful in the radiographic evaluation of mal or non-adaptive bone injury.

Magnetic resonance imaging

MRI is useful to evaluate bone and soft tissue abnormalities in the MTPJ and nearby structures. In fact, in some horse-dense locations such as Newmarket, England examination of the MCP/MTPJs using standing low-field MRI has become as commonplace as scintigraphic examination and often preferentially requested by TB trainers. In TB and STB racehorses with mal or non-adaptive bone remodeling of distal MtIII, MRI examination reveals extensive subchondral bone damage characterized predominately by low signal intensity of the plantar aspect of the lateral condyle of MtIII on T1 and T2-weighted images, a finding supporting the
existence of chronic, sclerotic subchondral bone. Within the areas of low signal intensity is often a small area of high signal intensity near the articular cartilage. In fat-suppressed and short tau inversion recovery (STIR) image sequences small, focal areas of high signal intensity within sclerotic bone are often found, indicating the presence of necrotic, and perhaps ischemic bone, but widespread areas of high signal intensity consistent with bone edema from acute trauma are not often seen. While numerous authors or speakers have characterized these lesions as bone bruises, bone edema (fluid accumulation) characteristic of bone bruises found in subchondral bone in people, is not a hallmark of this common lesion in horses. Areas of increased signal intensity within sclerotic subchondral bone in horses with repetitive stress injuries could represent proteinaceous fluid, but likely represent regions of necrotic bone or granulation tissue. Areas of necrotic bone seen on MR images correspond to radiolucent defects; areas of bone loss, necrotic subchondral bone or areas of intense resorption within sclerotic bone may warrant consideration when trying to manage horses with this lesion. In horses with acute onset clinical signs consistent with acute subchondral bone injury or fracture bone edema can be more prominent. In 13 horses, most of which were non-racehorses, with lameness of the MCP/MTPJs and without radiological abnormalities, the most common finding was decreased signal intensity in T1-weighted images indicating the presence of sclerotic subchondral bone. In 9 horses decreased signal intensity in T2-weighted images consistent with sclerosis, but 5 had increased signal intensity in fat suppressed and STIR images consistent with what was described as fluid accumulation within the sclerotic regions. Importantly, MRI abnormalities and subchondral bone lesions were found not only in racehorses but in horses used for show jumping and general purpose riding. Lesions similar to those described for racehorses were seen in the MTPJ of sports horses. Focal areas of IRU seen scintigraphically appeared in MR images as areas of low signal intensity on T1 and T2-weighted images with or without small areas of increased signal intensity in STIR images indicating the presence of chronic, repetitive stress injuries of distal MtIII exist in sports horses in addition to acute, traumatic injuries. In an earlier study of 11 horses, of which 8 were non-racehorses, that underwent MR imaging for subchondral bone damage with no or equivocal radiological abnormalities 4 had lesions in the MCPJ and the MTPJ. Horses with acute onset lameness had subchondral bone fluid accumulation characterized by increased signal intensity in STIR and T2-weighted images. In 2 horses decreased signal intensity in proton density images (similar to T1-weighted images) indicated the presence of sclerotic subchondral bone of distal MtIII but dense bone was surrounded by areas of increased signal intensity in STIR sequences. Only 2 horses had bone scintigraphy performed and areas of IRU in the damaged subchondral bone were seen. Horses with acute subchondral bone injury should improve with rest whereas those with chronic, sclerotic and osteoarthritic subchondral bone may improve temporarily with rest but long-term prognosis is guarded. MRI was also useful in the evaluation of horses with oblique and straight distal sesamoidean desmitis in 27 horses with lameness localized to the MCPJ/MTPJ region, of which 17 had lameness and injury in the hindlimb. Careful examination of soft tissue structures associated with the MTPJ, including use of diagnostic ultrasonographic examination, is necessary since in some horses results of diagnostic analgesia will be ineffective at differentiating authentic sources of pain in the region.
Computed tomography

Computed tomography (CT) is useful to characterize complex fractures of the MTPJ and to aid in pre-operative planning for surgical repair and to study other defects of articular surfaces. CT was superior to radiography in detecting articular comminution, small cracks and lucencies in the MtIII condyles, and fractures of the PSBs. However, orthogonal radiography was superior to CT in detecting fractures of the dorsal aspect of the proximal phalanx and both imaging modalities were poor at detecting plantar fractures of the proximal phalanx and coalescing cracks in the subchondral bone of MtIII. CT is not as useful as scintigraphy and MRI in the evaluation of subchondral bone injury.

Arthroscopic examination

Arthroscopic surgery is used frequently for removal of osteochondral fragments and fractures of the PSBs, assistance in fracture reduction and screw placement in horses with condylar fractures of the distal MtIII and fractures of the proximal phalanx, and lavage and debridement in horses with infectious arthritis. Diagnostic arthroscopic examination is indicated if lameness is localized to the MCP/MTPJ, but radiological findings are negative or suggestive of occult osteochondral fragments, but should be undertaken after evaluating the results of advanced imaging such as scintigraphic and MR imaging. Before routinely using scintigraphy I would often elect to evaluate the articular surface of the MTPJ arthroscopically, only to be disappointed in my inability to substantiate obvious abnormalities. Using scintigraphy and more recently MR imaging, I can often characterize injury of the joint without the need for diagnostic arthroscopy. The most common diagnosis is subchondral bone injury without obvious overlying cartilage damage, findings that obviate the need to examine the joint arthroscopically. Diagnostic arthroscopy is indicated if cartilage damage or osteochondral fragments are suspected, and to confirm the extent of cartilage damage in horses with OA. Occult fragments involving the proximodorsal aspect of the proximal phalanx are occasionally found. Cartilage damage, sometimes full-thickness, is found on the distal-dorsal aspect of the MtIII and proximal aspect of the proximal phalanx in non-racehorses. In racehorses with OA cartilage lesions are usually most pronounced in the plantar pouch, with extensive scoring or large areas of full-thickness damage and exposed subchondral bone on the PSBs. Although stress-related bone injury and later overlying cartilage damage is seen on the distal plantarolateral aspect of the MtIII, this area is difficult to evaluate during arthroscopic examination.

Bisphosphonate therapy for management of subchondral bone pain

The bisphosphonate drug, tiludronate, has received considerable attention in recent years for management of numerous lameness abnormalities, but while there are many anecdotal reports there is scant scientific evidence to support its use in the horse. Bisphosphonate drugs are largely antiresorptive and work by reducing osteoclastic activity. In mal or non-adaptive bone remodeling and in horses with more advanced OA the predominant process is one of bone accumulation; dense sclerotic bone develops in the subchondral plate and adjacent cancellous bone, so in theory a drug to reduce osteoclastic resorption might have a net effect of increasing bone formation. How and why would antiresorptive drugs work in predominantly sclerotic subchondral bone? Bisphosphonate compounds may help to normalize metabolism in bone injuries characterized by abnormal resorption and formation, such as that seen with navicular
disease, a disease with similarities to mal or non-adaptive remodeling of MtIII and other bones. Based on this theory, in a double-blind, placebo controlled study, horses with navicular disease given tiludronate at 1 mg/kg intravenously (IV), once daily for 10 days, had optimal improvement in lameness scores and returned to a normal level of activity 2-6 months after administration. Furthermore, horses with OA of the thoracolumbar vertebral column given the same dose of tiludronate showed significant improvement in dorsal flexibility compared to untreated controls. In horses, adaptive response to high-strain cyclic fatigue in the subchondral plate and adjacent subchondral bone occurs in response to race training. In a histologic study of TB distal Mt/McIII condyles site-specific increases in microcrack density in calcified cartilage and resorption spaces in the adjacent subchondral plate were interpreted as evidence of mechanical failure of the joint surface from progressive endochondral ossification and modeling/remodeling of subchondral bone. Propagation of microcracks into subchondral bone may be critical to the subsequent development of condylar fractures or OA. In sclerotic subchondral bone osteocyte morphology was abnormal and numbers reduced, but site-specific microdamage, targeted remodeling of adjacent subchondral bone, and multiple pathways of mechanotransduction of McIII were thought to be important in adaptation to exercise. In a study of 25 distal Mc III condyles of TB racehorses extensive microcrack formation leading to microfracture was found in sclerotic subchondral bone close to the calcified cartilage layer and the presence of osteoclastic resorption along microfracture lines was proposed to have caused previous weakening. In these studies the presence of resorption and bone weakening in calcified cartilage and adjacent subchondral bone may lend evidence to justify the use of bisphosphonate compounds, primarily for reduction in resorption and potentiating healing of microdamage. In people with OA of the knee, joint space narrowing and sclerosis of the nearby subchondral plate occurs, and sclerotic bone may act to stress-protect adjacent cancellous bone, called sub-articular bone, since vertical and horizontal trabeculae number were reduced resulting in bone loss. Using Fractal Signature Analysis to measure differences of cancellous bone density in osteoarthritic medial knee compartments in people, increased trabecular number associated with thinning and fenestration of trabeculae in sub-articular regions confirmed that overall, cancellous bone was osteoporotic. Osteoporosis, although not known to be found in horses with OA could potentially be managed using bisphosphonate therapy. Bisphosphonate therapy alone and in combination with estrogen therapy slowed early changes in subchondral bone architecture and reduced the prevalence of OA-related subchondral bone lesions. Given the presence of intense resorption at various sites and the presence of osteoporotic subchondral bone a case could be made for the administration of bisphosphonate drugs. Long term studies, and more double-blind, placebo-controlled studies need to be done.

Anecdotally, there may be benefit from use of tiludronate in horses with OA and subchondral bone injury but it makes most sense to combine the drug with rest or a modification in exercise to allow healing of microdamage. While lameness scores improved in horses with navicular disease, my limited experience in horses with subchondral bone pain of distal MtIII, suggests amelioration of lameness is subtle and long-term evidence of benefit cannot be established. The drug can be used IV, at a dose of 1 mg/kg in a single infusion or divided over 10 days for a total dose of 1 mg/kg, since both dosage regimens resulted in similar plasma exposure and pharmacologic effects. There has been a trend to administer the drug to horses with single distal limb lesions using intravenous regional limb perfusion techniques, but this
technique would be impractical in horses with numerous abnormalities involving more than a single limb, and has not been studied. Use of the drug and continued training and racing may potentially lead to condylar fracture or other further injury particularly in TB racehorses, a sequel that should be strongly considered. Currently I believe targeting areas of bone resorption or necrosis, relative osteoporosis, and attempting to normalize subchondral bone formation and healing using bisphosphonate therapy in combination with a reduction in exercise intensity is a reasonable approach, particularly in horses with bilateral hindlimb subchondral bone pain (or more numerous abnormalities). I prefer a single slow, IV infusion (1 mg/kg) and warn owners and trainers about the limited collective knowledge of complications in the horse and of the known complication of osteonecrosis of the jaw associated with bisphosphonate use in people.\textsuperscript{31} Anecdotally, while bisphosphonate therapy appeared trendy and popular in the last few years, recently it appears that the undertone is that this medication is not particularly useful either in subchondral bone injury or other clinical conditions for which it has been used.

\textit{Surgical management of subchondral bone injury}

In 3 racehorses, I have used the surgical technique of subchondral perforation (forage). The 2 TBs and 1 STD had unilateral hindlimb lameness in which lateral plantar metatarsal analgesia abolished lameness (horses did not show lameness in the contralateral hindlimb after blocking the principal limb), bone scintigraphy identified focal IRU of the distal, plantarolateral aspect of MtIII, and in the 1 horse MR imaging showed typical subchondral bone injury of the lateral MtIII condyle. Arthroscopic examination of the plantar aspect of the metatarsophalangeal joint in all horses revealed normal appearing articular cartilage, and using a combination of needles preplaced along the plantar aspect of MtIII under arthroscopic guidance and intra-operative fluoroscopy, 3, 3.5 mm holes were drilled in a lateral-to-medial direction through the plantar aspect of the lateral MtIII condyle. Drill holes extended past the axis of MtIII into but not through the medial condyle. Horses were given 4 months of rest before returning to training. The rationale for this approach is similar to what is done in horses with dorsal cortical fractures of McIII, in which, osteostixis is performed. Subchondral forage may allow marrow components from the medial condyle and adjacent lateral condyle to repopulate and heal damaged subchondral bone and there may be immediate decompression of painful, sclerotic subchondral bone. All 3 horses raced after surgery but in 1 TB lameness recurred after 2 race starts. An alternative surgical approach of inserting a positional or set cortex bone screw may make theoretical sense.

\textit{Recent evidence}

A new description and terminology for subchondral bone injury, cumulative stress-induced bone injury, was published along with recommendations and results in a group of TBs with this injury of the distal aspects of the McIII and the MtIII.\textsuperscript{32} There were more males than females and there was no difference between pre and post diagnosis total earnings, but earnings/start decreased significantly.\textsuperscript{32} Sixty-two percent of horses raced at the same or lower race class.\textsuperscript{32} Paddock turn out exercise was prescribed and free-choice exercise of at least 60 days was thought to be important for healing and rehabilitation.\textsuperscript{32} More recently, a study detailing the scintigraphic abnormalities of TB racehorses with IRU of the distal aspects of the McIII and MtIII, reported results that appear to mirror my experience with this important injury.
Increased radiopharmaceutical uptake of the palmar condyles of the McIII and the plantar condyles of the MtIII was identified in 103 of 220 horses and occurred most commonly palmaromedially and plantarolaterally. Affected horses were compared to a cohort (controls) and had significantly fewer starts, reduced earnings and reduced earnings/start than controls. It has also been my experience that subchondral bone injury is chronic, recurrent and takes a toll on horses’ success and earnings potential after diagnosis; while horses can race, they race in a lower race class, have fewer earnings/start and reduced racing longevity.