Technetium-99 m-HDP uptake characteristics in equine fractures: A retrospective study

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Summary

Bone scintigraphy is a very sensitive diagnostic tool to detect elevated bone metabolism. In cases of fractures and fissure fractures, the radiopharmaceutical uptake in the bone is said to be increased within a few hours after the injury. In this retrospective study, the scintigraphic uptake characteristics at the fracture site of 36 horses with radiographically confirmed fractures or fissure fractures were evaluated. Uptake ratios between the fracture region and adjacent normal bone or soft tissue activity respectively were calculated and compared to different anamnestic and radiographic data. The overall sensitivity of bone scintigraphy was 94.4% (34 positive cases out of 36). In the 36 horses, no correlation between the age of the fracture and the radiopharmaceutical uptake was found. However, there seems to be a lack of sensitivity in early detection of equine pelvic fractures when a standing bone scintigraphy examination protocol is used.

Keywords: horse, fracture, bone scintigraphy, uptake ratio

Anreicherungsverhalten von Technetium-99 m-HDP bei Frakturen des Pferdes: Eine retrospektive Studie

Die Knochenszintigraphie ist ein sehr sensitives diagnostisches Verfahren, um eine erhöhte Knochenumbaurate nachzuweisen. Bei Frakturen und Fissuren ist die Speicherung des Radiopharmakons schon wenige Stunden nach dem Trauma erhöht. In dieser retrospektiven Studie wird das Anreicherungsverhalten in der Frakturregion bei 36 Pferden mit radiologisch bestätigter Fraktur oder Fissur evaluiert. Der Speicherquotient der Technetiumverbindung zwischen der Fraktur und dem umliegenden normalen Knochen, respektive der Weichteile, wurde berechnet und mit verschiedenen anamnestischen und radiologischen Daten verglichen. Die Sensitivität der Knochenszintigraphie betrug in dieser Studie 94.4% (34 von 36 Fällen positiv). Es konnte keine Korrelation zwischen dem Alter der Fraktur und der Anreicherungsintensität der Radiopharmakons gefunden werden. Bei der szintigraphischen Frühuntersuchung von Beckenfrakturen am stehendem Tier wurde jedoch eine niedrige Sensitivität festgestellt.

Schlüsselwörter: Pferd, Fraktur, Knochenszintigraphie, Speicherquotient

Introduction

Bone scintigraphy is a widely used imaging tool in the diagnostic work up of equine orthopaedic disorders. The advantages of this technique consist of a relatively low invasiveness, an excellent screening capacity and a high sensitivity in diseases presenting with abnormal bone metabolism. The bone activity is said to increase within the first seven hours after an accident with a concurrent bone fracture (Rosenthall, 1976; Ueltschi, 1980) because of the elevated bone metabolism. If three days after the injury increased bone activity is not present, a fracture can be excluded with high probability (Ueltschi, 1980).

In this retrospective study the authors wanted to evaluate the sensitivity of equine bone scintigraphy in early fracture detection in different skeletal regions. Furthermore, the factors influencing the scintigraphic sensitivity of radiographically confirmed fractures should be examined.

Animals, Materials and Methods

A retrospective search of all equine patients, that underwent a bone scintigraphy at the Division of

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Clinical Radiology of the Department of Clinical Veterinary Medicine of the University of Berne between January 2000 and March 2006 was conducted. A total of 36 patients with radiographically confirmed bone fracture or fissure fracture were included in the study, and no other in-or exclusion criteria were defined. Case history, signalement of the horse, age and localisation of the fracture, scintigraphic and radiographic fracture findings and position of the horse during scintigraphy (either standing under sedation, or recumbent under general anaesthesia) were retrieved from the medical records. If the data concerning the history were incomplete or unclear, the owner was contacted by phone.

The radiographs were assessed considering the following criteria: a) extent of a fracture (for example complete or incomplete), b) amount of dislocation of fracture fragments and c) description of callus formation. The radiopharmaceutical uptake intensity and pattern at the fracture site, which was derived from the corresponding radiographs, were described subjectively. The lesions were classified as having either a normal or an increased radiopharmaceutical uptake, or an abnormal radiopharmaceutical uptake pattern. The latter group consisted of patients without a distinctly increased uptake but with a change in the shape of the fractured bone or a site next to the fracture region with increased uptake (Fig. 1). Regions of interest (ROIs) were drawn manually in the fracture region, again derived from the radiographic localisation. A region of interest was also drawn manually in the surrounding soft tissue in pelvic fractures and in adjacent normal bone in appendicular skeletal fractures respectively. If bone scan images of the non-affected contralateral regions were available, ROI's were also drawn manually at the identical contralateral localisations. In some cases the affected and non-affected contralateral body parts were on the same bone scan image, which allowed to draw all the desired ROIs on one single image. The uptake ratio was calculated with the average pixel activity (counts/pixel) of the fracture site divided by the average pixel activity of soft tissue or the adjacent normal bone, respectively; similar to the method described in the literature (Geissbühler et al., 1998). These ratios were then compared to the above mentioned parameters of signalement of the horse, fracture age according to the history, and to the radiographic and scintigraphic findings.

Basic descriptive statistics and figures were generated using NCSS 2004 (www.ncss.com). For comparison of continuous measurements between recumbent and standing horses, box plots and the Kruskal-Wallis ANOVA on Ranks were used. To assess the joint influence of position of the horse and the fracture region on pharmaceutical uptake ratio, a 2-way ANOVA was run. Correlation between uptake ratio and the age of the fracture was evaluated with the Spearman Rank correlation coefficient (r). The alpha level of statistical significance was set to 0.05.

Results

The 36 patients had a mean age of 9.1 years (range 3–20 years). The population consisted of 30 Warmblood, 2 Thoroughbred and 4 Coldblood horses. 17 horses were geldings, 15 mares and 4 patients were stallions. No associations between age, breed and sex of the horses and the measured radiopharmaceutical uptake were found. Stallions showed a tendency of higher intensities at the fracture sites. 14 horses suffered from a pelvic fracture, 8 out of them were fractures of the ischiatic tuberosity, 5 of the pelvic ring and 1 of the tuber coxae. 20 patients had limb frac-

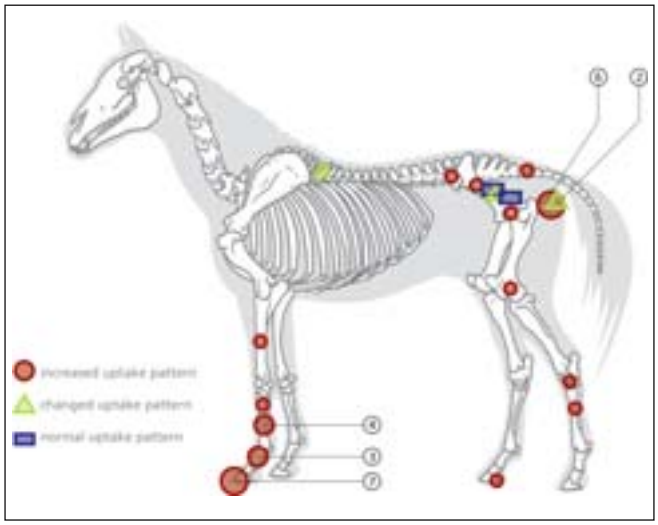

Figure 1: Graphic representation of the equine skeleton demonstrating the distribution and frequency of the fracture cases of this study. The numbers at the larger symbols indicate the total number of cases of the marked body region. The small symbols without a number are representing one single case each.

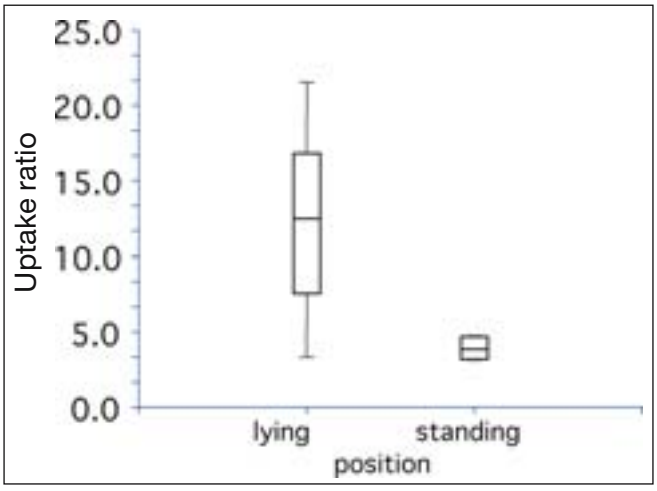

Figure 2: Influence of the position (recumbent/standing) during bone scintigraphy of horses with pelvic fractures on the uptake ratio ($p = 0.068$).

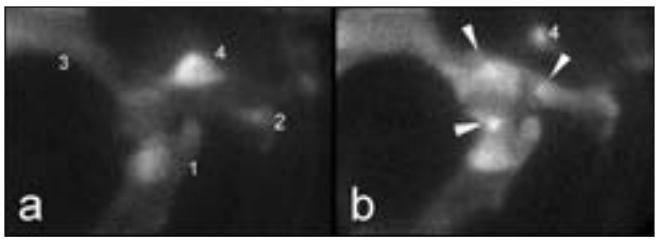

Figure 3a, b: Bone scans of a horse with a 7-day-old comminuted right sided pelvic fracture; the examination was conducted in lateral recumbency.
a: oblique view of the pelvic region from left laterocaudodorsal
b: oblique view of the pelvic region from right laterocaudodorsal; diffusely increased radiopharmaceutical uptake in the fractured acetabular region (arrow heads)
1 caudal part of the major femoral trochanter, 2 ischiatic tuberosity, 3 Os ilium, 4 bladder

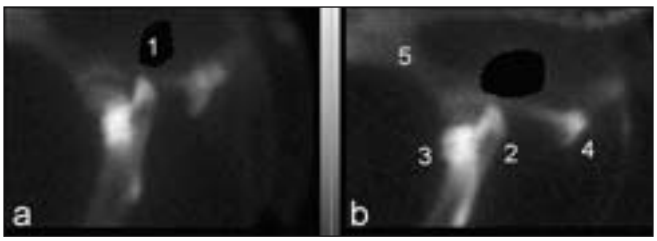

Figure 4a, b: Laterocaudodorsal oblique bone scans of a horse with an old (> 365 days) fracture of the left ischiatic tuberosity; the examination was performed in lateral recumbency. Figure a (left hemipelvis) shows an altered shape and size of the ischiatic tuberosity, but no increased radiopharmaceutical uptake; Figure b: normal right hemipelvis.
1 masked bladder activity, 2 caudal part of the major femoral trochanter, 3 cranial part of the major femoral trochanter, 4 ischiatic tuberosity, 5 Os ilium

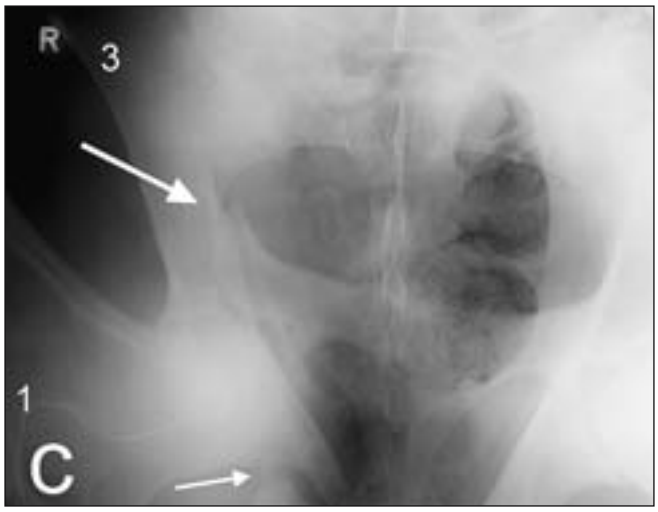

Figure 3c: Ventrodorsal radiograph of the pelvis of the same horse as in Figure 3a and b. The arrows point at the pelvic fractures.

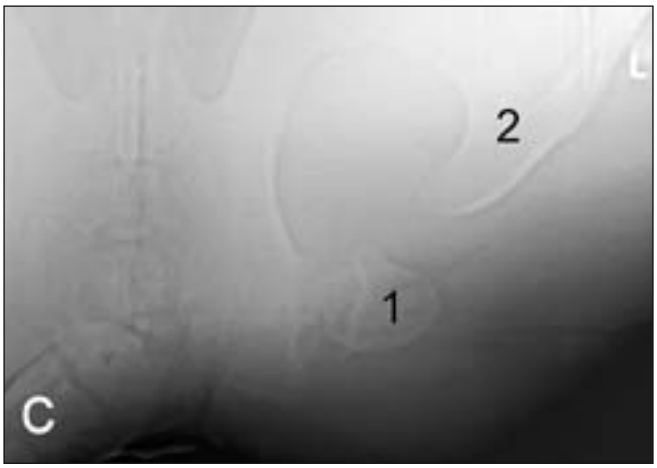

Figure 4c: Ventrodorsal radiograph of the caudal part of the left hemipelvis with the coxofemoral joint in flexed position; same horse as in Figure 4a and b.
1 fractured left ischiatic tuberosity, 2 caudal part of the left major femoral trochanter

tures; 17 of them were localised distally to the carpus or tarsus. 2 horses had a fracture of the spinal process and of a coccygeal vertebra respectively (Fig. 1).

According to the history, the median age of the fracture was 42 days (range 1–365 days, 365 days for all the fractures, which were one year old or older). The median age for the pelvic fracture was 45 days (range 1–365). The median age for the limb fractures was 42 days (range 10–365), in 3 horses with pelvic fractures and in 2 horses with limb fractures the anamnestic age of the fracture was not known. There was no significant correlation between the age of the fracture of all regions combined and the uptake ratio ($r = -0.14$; $p = 0.44$). Pelvic fractures had a moderately positive correlation between the age of the fracture and the uptake ratio ($r = 0.38$; $p = 0.21$); younger fractures were less active than older ones. 12 horses with pelvic fractures underwent the scintigraphic examination in lateral recumbency and 2 in an upright position under sedation. There was a tendency to higher uptake ratio in pelvic fractures with an examination protocol in lateral recumbency (median = 12.55) when compared to standing (3.94; $p = 0.068$) (Fig. 2).

14 horses with limb fractures were examined in a standing position, 6 out of the twenty patients were under general anaesthesia during scintigraphy. There was no significant difference between the uptake ratio in standing (2.32) and recumbent (1.95) horses with fractures of the appendicular skeleton ($p = 0.75$). 9 horses with pelvic fractures had an increased uptake in the fracture region (Fig. 3a–c). 3 horses with pelvic fractures had increased uptake and/or an abnormal uptake pattern. In 1 of them the hot spot was not localised at the fracture site and in the other two cases, a deformation of the pelvis was visible on the bone scan images (Fig. 4a–c). 2 horses with pelvic fractures had a normal uptake pattern (Fig. 5a). Both horses were examined in an upright position. From one of these two horses, radiographs were taken the day after the scintigraphic exam. The second horse without increased uptake was treated conservatively for several

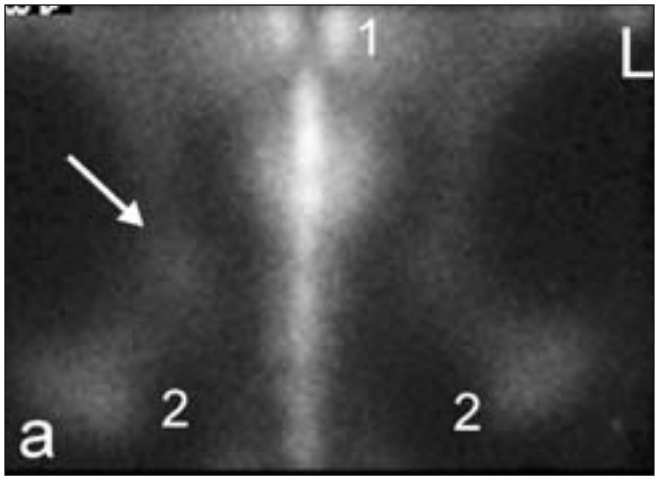

Figure 5a: Dorsal bone scintigram of a horse with a 5-day-old pelvic fracture; the bone scan was taken in standing position. No left-right asymmetry in the radiopharmaceutical uptake is visible. The uptake pattern is normal. The arrow points to the right coxofemoral joint (fracture site).
1 left sacroiliac joint, 2 ischiatic tuberosity

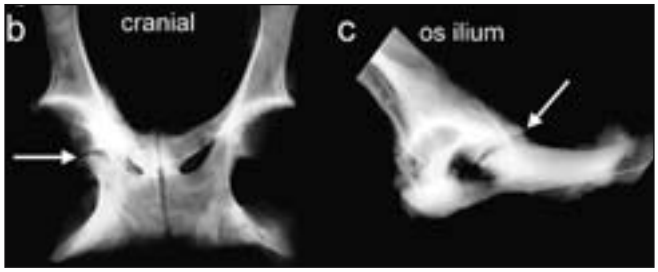

Figure 5b, c: Ventrodorsal and laterolateral radiographs of the pelvis of the same horse as in Figure 5a; the radiographs were taken at the post mortem examination, 47 days after the bone scintigraphy. The arrows indicate the fracture lines and the pronounced callus formation in the right caudal acetabular aspect.

weeks, before the diagnosis of a pelvic fracture was made by clinical examination. Radiographs of this horse were taken at the post-mortem examination and revealed fractures of the os ischium and os pubis (Fig. 5b, c). The 20 horses with limb fractures all showed increased uptake ratios in the fracture region (Fig. 6a–c). The same was noticed in the horse with the fracture of the coccygeal vertebra. In the horse with the fracture of the spinal process, an abnormal shape was visible on the bone scan image, but there was no increased uptake of the radiopharmacon.

The fractures of all 14 horses with pelvic fractures and of 16 out of 20 patients with limb fractures were complete. There was no association between the extent of the fracture and the uptake ratio for both groups (median = 3.37 for complete fractures, 2.99 for incomplete fractures). 18 horses had no dislocation of the fracture fragments, one of those belonging to the pelvic group. 5 horses out of 18 with distinct dislocation of fragments had limb or vertebral fractures. Horses with dislocation of the fracture fragments (median = 7.5) had a significantly higher uptake ratio than the horses without any dislocation (median = 2.25, $p < 0.001$) (Fig. 7).

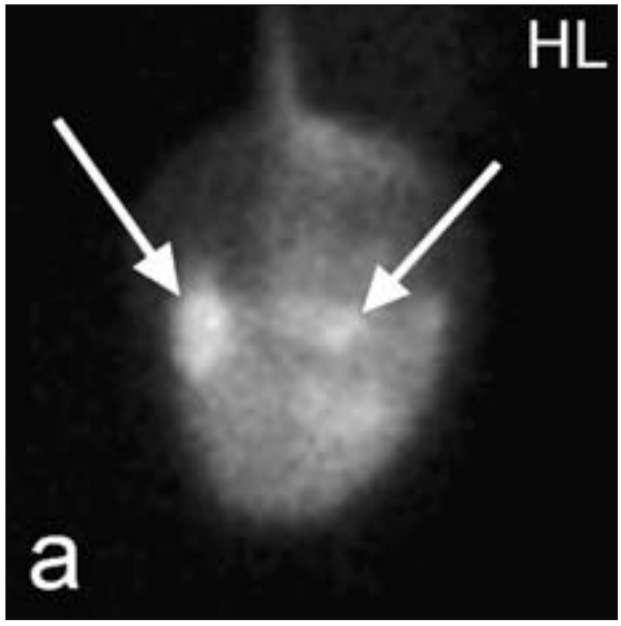

Figure 6a: Solear bone scan of the distal phalanx of the left hindlimb, examined in general anesthesia. The horse suffered from a 180 days old fracture of P3 and of the navicular bone. The arrows indicate two regions with increased radiopharmaceutical uptake, one in the medial branch of P3, another in the area of the navicular bone. A third focally increased uptake exists further dorsally, slightly lateral to the median plane.

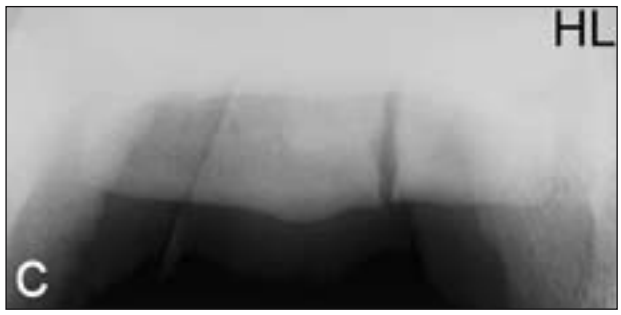

Figure 6b, c: Dorsal 60° proximal-plantarodistal oblique radiograph of the left distal phalanx (b) and plantar 45° proximal-plantarodistal oblique view of the left navicular bone of the same horse as in Figure 8a. There exists a sagittal fracture of the lateral aspect of the navicular bone with unsharply defined fracture ends and an oblique fracture at the base of the medial branch of P3 with an irregular course of the fracture line (6b, white arrowheads).

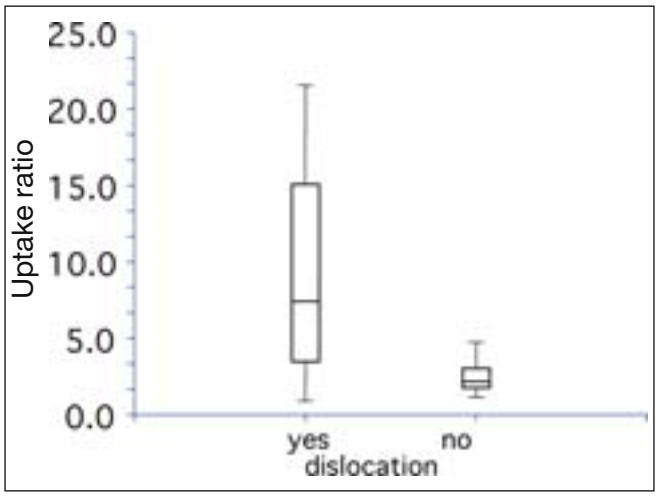

Figure 7: Horses with a dislocated fracture have significantly higher uptake ratios than horses without dislocation ($p < 0.001$).

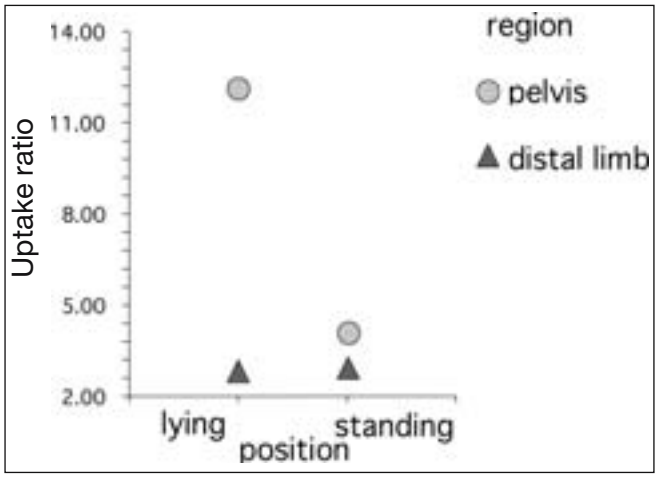

Figure 8: The diagram shows the influence of the position during the scintigraphic exam and the fracture site on the pharmaceutical uptake ratio (position $p = 0.032$; region $p = 0.005$; interaction between region and position $p = 0.028$).

24 horses had no signs of callus formation, 10 of them with pelvic fractures and 14 horses with limb fractures. The other 12 horses showed classical signs of callus, 6 of them with limb fractures, 4 with pelvic fractures and the two horses with vertebral column fractures. No association could be made between callus formation and the uptake ratio ($p = 0.85$). When analysing the joint effect of position of horse and localisation of fracture on the uptake ratio, pelvic fractures showed a significantly decreased activity when standing while there was no difference between recumbent and standing position in distal limb fractures (position $p = 0.032$; region $p = 0.005$; interaction between region and position $p = 0.028$) (Fig. 8).

Discussion

In the present study, the authors were especially interested in the correlation between the scintigraphic protocol, the age of a fracture and the uptake of the radiopharmacon. Bone injury results in an immediate increased bone metabolism by increased blood flow at the fracture site, increased vascular permeability (activation of the inflammatory cascade), increased activity of osteoblasts and formation of new bone (Lamb und Koblik, 1988) and therefore in an increased radiopharmaceutical uptake, which can be recognised already seven hours after a fracture occurred (Rosenthall, 1976; Ueltschi, 1980). The radiopharmacon (Technetium-99 m-labeled HDP) binds to the inorganic component of the bone (hydroxyapatite crystal). At higher rates of blood flow, the uptake of the radiopharmacon is determined by the available crystal surface area. Therefore, intense activities, as seen at fracture sites, are associated with bone remodelling (formation and resorption), as it occurs during the healing period of a fracture (Lamb und Koblik, 1988). If three days after an injury still no increased uptake of the radiopharmacon can be detected, a fracture can be excluded (Ueltschi, 1980). Furthermore it has been described, that the level of activity progressively declines over the following 2–3 months (Dyson and Martinelli, 2003; Head, 2003) without mentioning the time point with the maximum uptake. Bessler (1967) says that after 12–24 months, the uptake pattern at the fracture site is normal again. In the present study – with a small number of cases – no correlation could be made between the age of the fracture and the radiopharmaceutical uptake, if all fracture locations are considered. However, two pelvic fractures revealed a negative scintigraphic result with normal amount of uptake and normal uptake pattern of the radiopharmacon. Both fractures were less than 1 week old (1 and 6 days). Also if callus formation, which is another indicator for the age of a fracture, was compared with the uptake ratios, no correlation was evident. One problem in this study was, that the age of the fracture was not always precisely known, especially in cases with an incidental fracture detection, such as in most splint bone fractures.

Additionally, a considerable number of other factors have an influence on the uptake of the radiopharmacon and on the bone scan image. Some factors originate from the horse itself like the local and systemic blood flow (Lamb und Koblik 1988), shielding of the photons by overlying muscle mass, delayed activity of the osteoblasts or "stealing" of pixel counts by a filled urinary bladder (Dyson and Martinelli, 2003; Head, 2003) during the examination of the pelvic region. Other factors originate from the examination procedure like the sensitivity and the specificity of the collimator and the examination time per scan (number of totally acquired counts), which is directly related to the position of the horse during the exam: In a horse under general anaesthesia, collimators with higher spatial resolution will be used,

which leads to increased image quality and longer scan times.

Our two cases of fresh pelvic fractures with normal radiopharmaceutical uptake were examined in an upright position. The reason for the false negative results may include fracture age, fracture location with a shielding effect of the muscle mass, and, as further important factor, the examination protocol (upright position with associated motion, slightly increased distance of the collimator to the horse, high sensitive collimator). It is debateable, if a pool phase examination would have demonstrated an increased soft tissue uptake in these two cases. For these two horses, the risk of a procedure under general anaesthesia and the risk of additional injury or breakdown during the recovery phase were considered to be too high and a standing protocol was used. Two additional horses with pelvic fractures of 2 and 7 days of age, respectively, were examined scintigraphically under general anaesthesia. Both horses showed increased uptake at the fracture site (Fig. 3). Both horses were examined in lateral recumbency, and both horses were euthanized under general anaesthesia immediately after fracture detection. In an additional 3 horses with pelvic fractures, a changed uptake pattern was seen without increased uptake at the fracture site. Scintigraphic identification of the fracture location therefore was difficult, and was depending on the recognition of abnormal distribution of activity within the bone rather than a hot spot. In these three cases, the fracture age and shielding effects of the pelvic musculature may have contributed to the non-specific scintigraphic findings.

In horses with acute limb fractures, the risk of a false negative scintigraphic result in a standing examination protocol seems to be low, and we think that this is mostly due to the lack of muscular mass covering the bone and therefore the lack of shielding the gamma-rays by the musculature.

In the present population only one horse suffered from a complete fracture of one of the weight bearing long bones of the appendicular skeleton (fracture of radius). It seems to be very likely, that in general such fractures are already detected on the base of a clinical examination (swelling, skin laceration, history, high grade lameness) and of concurrent radiographs. A scintigraphic exam therefore is rarely necessary in these cases.

Some of the fractures – mostly splint bone fractures – were incidental findings without clinical significance. As they showed an increased uptake of the radiopharmacon, radiographs were taken of the specific region. We are aware that the population is quite inhomogeneous including fractures of all body regions and of any fracture age. With the selection criteria used in this study some important scintigraphic differences between pelvic and appendicular skeletal fractures became obvious. The most important conclusions from this study are the fact that negative scintigrams do not exclude acute pelvic fractures and chronic fractures may present a changed pattern rather than a clear hot spot. For acute pelvic fractures, image quality and therefore the position of the horse during scintigraphic examination seems to play an important role. In cases of suspicion of an acute pelvic fracture with a normal uptake in the scintigraphic exam, it might be recommended to repeat the exam after 10–14 days, to take oblique radiographic views of the pelvis in an upright position, as described by Hornof et al. or to try to come to a diagnosis by rectal or transcutaneous ultrasonography (Reef, 1992; Shepherd and Pilsworth, 1994; Sheperd et al. 1994). More cases – in retro- or prospective studies – would be needed to obtain more reliable results.

Particularité de l'incorporation des traceurs radioactifs lors de fractures chez le cheval: étude rétrospective

La scintigraphie osseuse est une technique diagnostique très sensible qui met en évidence un métabolisme augmenté dans l'os. Dans les cas de fractures et des fissures, l'incorporation du traceur radioactif est augmentée déjà peu d'heures après le traumatisme. Dans cette étude rétrospective, on a évalué cette incorporation caractéristique dans la zone de fracture sur 36 chevaux présentant une fracture ou une fissure confirmée radiologiquement. L'incorporation du technétium dans la zone de fracture,

Proprietà dell'incorporazione di radiofarmaci in fratture nei cavalli: studio retrospettivo

La scintigrafia ossea è un procedimento diagnostico altamente sensibile per evidenziare un aumento di metabolismo nelle ossa. Già poche ore dopo il trauma, l'incorporazione del radiofarmaco è aumentata in caso di fratture e fessure. In questa retrospettiva è stata valutata, su 36 cavalli che presentavano una frattura o fessura confermata radiologicamente, l'incorporazione caratteristica della zona fratturata. L'incorporazione del composto di tecnezio nella zona della frattura, nella regione

dans l'os sain environnant ainsi que l'activité dans les tissus mous a été calculée et comparée avec diverses données anamnestiques et radiologiques. La sensibilité de la scintigraphie osseuse s'élevait dans cette étude à 94,4% (34 cas positifs sur 36). On n'a pas pu mettre en évidence de corrélation entre l'âge de la fracture et l'incorporation du traceur. Un examen précoce sur animal debout dans les suspicions de fractures du bassin n'est toutefois que moyennement indiqué, sa sensibilité étant plus basse que dans un protocole avec animal couché.

ossea normale attinente e nell'attività dei tessuti molli è stata calcolata e paragonata con diversi dati anamnetici e radiologici. La sensibilità della scintigrafia ossea tocca in questo studio il 94.4% (34 casi positivi su 36). Non si è potuta provare la relazione tra l'età della frattura e l'incorporazione del radiofarmaco. Un esame scintigrafico precoce sull'animale in stazione eretta in caso di fratture del bacino non è che parzialmente indicata poiché la sua sensibilità è meno elevata che per un protocollo di un animale in posizione sdraiata.

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