4 Imaging of Insufficiency Fractures

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Abbreviations

CT Computed tomography
MRI Magnetic resonance imaging
SPIR Selective partial inversion recovery
STIR Short-time inversion recovery
TNF Tumor necrosis factor

4.1 Introduction

Insufficiency fractures are a subgroup of stress fractures, caused by normal stress on weakened bone with an impaired elastic resistance due to alterations in density or structure. Fatigue fractures, on the contrary, are caused by abnormal stress on a regularly dense and structured bone with normal elastic resistance.

Bone is a highly dynamic and constantly remodeling tissue which needs continuous mechanical stress by weight and muscular action to develop correctly. To understand the biomechanical mechanisms underlying the particular forms of fractures, it is necessary to define "stress." In normal loading conditions, both the bone mass and the turnover are physiologically maintained by a coordinated balance of bone formation by osteoblasts and bone resorption by osteoclasts. When the bone is unable to sustain or to respond to a normal stimulus, or when the stimulus is reiterated and abnormal but not physiological, an imbalance can occur that favors the osteoclastic activity. A typical example is nonuse

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atrophy, which occurs after prolonged immobility; the lack of burden activates the osteoclasts to reabsorb the bone. In contrast, with a repeated, excessive, or incongruous stimulus, such as a sudden increase in the exercise load for an athlete, the stress-related microdamage cannot be adequately repaired. The osteoclastic resorption works faster than the remodeling mechanisms of new bone formation; with consequent weakening and structural fragility, the bone cannot resist incongruous stress. Although this process can be moderate and reversible at the beginning, the stress response is characterized by edema and periosteal reaction; if the condition persists, the normal mechanism of bone repair becomes inadequate, setting the stage for a fatigue fracture.

Any pathological condition that causes a decrease in both bone elasticity and bone resistance can be a predisposing factor for insufficiency fractures (Cummings and Melton 2002).

A far more common cause of quantitative and qualitative alterations of micro- and macro-bone structure, particularly in older people, is osteoporosis, followed by less frequent causes such as rickets, osteomalacia, rheumatoid arthritis, hyperparathyroidism, Cushing disease, Paget disease, thesaurismosis, or rare metabolic disorders.

Additional causes of bone structure weakening are continuous intake of steroids or irradiation.

Insufficiency fractures are associated with high mortality and significant morbidity, as well as with high economic cost: more than 200 million people, 75 million of them in Europe, the USA, and Japan, are affected by osteoporosis. Currently, every year in Europe and the USA, about 2.5 million fractures are ascribed osteoporosis. In 1990, the estimated number of femur fractures worldwide was 1.6 million, but they are expected to increase to 6.3 million by 2050. The economic and social consequences attributable to fractures in patients affected by osteoporosis are extremely severe and are estimated to reach several billion dollars per year.

Mortality is mainly associated with fractures of the femoral neck and, to a lesser extent, with vertebral fractures, although some part of the mortality has to be more reasonably attributed to generally poor condition as well as to prolonged immobility rather than to the fractures themselves.

On the whole, the death risk increases by 10–20 % in people with a fractured femur compared to the general population (Melton 2003).

Femur fractures cause different degrees of impaired ambulation in about half of the people affected. It is possible to observe in these subjects an overall decline in health, together with a higher risk of pulmonary embolism. About 30 % of patients become unable to perform everyday activities and are totally dependent on nursing care and in some cases even require hospitalization.

These fractures have to be mainly attributed to primary postmenopausal osteoporosis (type I): it has been noted that more than 25 % of postmenopausal women are at risk of vertebral fracture.

The incidence of insufficiency fractures attributable to senile osteoporosis (type II) is lower in men than in women, although still very high. The higher incidence of these lesions in women is due both to type I osteoporosis and to their longer life expectancy. From a pathogenetic point of view, both the osteoblasts, the cells responsible for bone production, and the osteoclasts, responsible for bone resorption, are controlled by parathyroid hormone, calcitonin, estrogens, and vitamin D.

Postmenopausal type I osteoporosis occurs in patients aged 50–70 years and is statistically six times more common in women than in men; it can occur in men with low levels of serum testosterone and loss of gonadal function. In peri- and postmenopausal women, decreased estrogen production causes a severe thinning of bone tissue coupled with an increase in cytokine levels such as interleukin-1, TNF, and interleukin-6, which are thought to produce an increase in osteoclast precursor recruitment and activity within the trabecular bone. These physiopathological considerations are confirmed when observing the fracture sites: type I osteoporosis is mainly responsible for fractures of predominantly trabecular bones, such as the collapse of vertebral bodies. Senile, type II, osteoporosis is associated with normal age-related degenerative processes. The number of osteoblasts decreases, thus favoring osteoclast activity and a progressive decline of bone quality. This pathology occurs in the sixth decade, with higher prevalence in women than men. Senile osteoporosis damages both cortical and trabecular components, thus causing fractures of the femoral neck, pelvis, vertebrae, proximal humerus, and tibia. The mechanisms underlying this pathology are not fully understood, as the condition may be caused by both decreased synthesis of vitamin D, which often occurs in the elderly, and resistance to vitamin D-related effects, most likely due to alterations of the receptor profile. In old women, both events are common. Calcitonin levels are unlikely to be involved in senile osteoporosis.

Obesity seems to be associated with higher bone mass, as are late menarche, early menopause, overconsumption of caffeine and alcohol, and tobacco use, all of which are thought to be predisposing factors. Genetics also play an important role, as clear family patterns exist, yet no evidence of inheritance has been provided so far.

Insufficiency fractures often localize in specific regions, as a function of pathological conditions and biomechanical factors, which account for the more frequent occurrence of this phenomenon in vertebral bodies, the pelvis, and the lower extremities, where biomechanical stress is most severe.

The main goals of imaging insufficiency fractures are correct recognition of the lesion, differentiation from fractures secondary to other diseases, and identification of the underlying pathology. Insufficiency fractures are typically characterized by localized pain, soft tissue edema, heat, and functional impairment of different degrees depending on the fracture site. However, as these symptoms also result from other types of fractures, they are not specific to insufficiency fractures. Radiographic imaging plays a crucial role in the correct characterization of the patient's pathological condition. Indeed, the location and the radiographic characteristics of the fracture are often enough to identify the pathology and to determine management. In some cases, second-level techniques and methods are advised.

Osteoporotic fractures more often occur in the vertebral bodies, mainly in the thoracolumbar tract, femoral neck, sacrum, acetabulum, pubic symphysis, distal radius, tibia, calcaneus, and ribs. Senile osteoporosis more often involves the axial skeleton than type I. Frequently, patients with osteoporosis suffer from multiple fractures, which often date back to different periods; in fact, the risk of developing new bone lesions is extremely high (50–100 %) in osteoporotic patients with an existing fracture.

In oncology patients, it is necessary to distinguish between pathological fractures in bones affected by metastatic processes and insufficiency fractures in subjects undergoing pelvic tumor targeting radiotherapy, the latter mainly involving the sacrum and the pelvis.

Paget disease is a pathological condition associated with an increased incidence of insufficiency fractures and involves tubular bones of the lower limbs. The lesions can occur during both the lytic and the sclerotic phase. The physiopathological reason underlying the increasing occurrence of fractures is the structure of the bone tissue, which is no longer adequate to the axial load and is deformed until it ruptures.

Another pathological condition associated with an increased risk of developing fractures is rheumatoid arthritis, a disease which is more frequently diagnosed nowadays than in the past. Fractures caused by rheumatoid arthritis mainly involve the pelvis and lower limbs.

An excess of corticosteroids is an iatrogenic condition that results in both density reduction and alteration in bone structure quality, as well as many metabolic disorders that cause secondary osteoporosis; the fracture sites are largely the same as primary osteoporosis. There are specific differences, however, such as a typical sign of osteomalacia, known as Looser lines, and focal accumulations of osteoid which appear as transverse radiolucent lines perpendicular to the cortical bone and are bilateral when observed in scapulae, ribs, pubis, and long bones.

4.2 Imaging Insufficiency Fractures

4.2.1 Radiography

In the weeks following an insufficiency fracture, radiology is severely affected by false negatives, depending on the injured area, age, and general conditions of the bone. Moreover, the sensitivity of radiography is quite low, ranging from 15 to 50 % (Guglielmi et al. 2003).

In addition, it should be noted that in the fractured bone, radiographic signs of osteopenia may remain hidden for a long period, as 30–40 % of the bone can be lost before osteopenia becomes evident. The correlation between painful functional symptoms and the underlying metabolic pathology, such as osteoporosis, may not be clear immediately.

However, during the early phases, some cases showing radiotransparent fracture line have been associated with an interruption of the cortical bone. Sometimes, evident osteopenia may hide the transparency of the fracture, thus hampering the radiographic examination. An actual fracture line is frequently absent, as it happens in the early phases of vertebral failures. Indeed, invisible trabecular microfractures may underlie slight bone deformations.

A lamellar periosteal reaction may be an early sign; it may appear particularly evident in contrast to advanced osteoporosis-related subperiosteal cortical resorption. More frequently, the fracture later appears as a sclerosis line, without evident signs of cortical rupture. Insufficiency fractures are often perpendicular to the long axis of the bone (Guglielmi et al. 2003).

Some fractures have specific properties; for example, those produced by an excess of corticosteroids typically develop a very hypertrophic bone callus.

4.2.2 Bone Scintigraphy

Bone scintigraphy is a sensitive tool for identifying insufficiency fractures, as it can detect very recent lesions that take weeks to become evident on radiographs. Moreover, scintigraphy can explore the whole skeleton at one time, identifying even clinically silent fractures. However, bone scintigraphy's specificity is rather low: frequently, it is not possible to exclude neoplasia as a cause of the abnormal accumulation without the help of other diagnostic tools. In technetium-99m diphosphonate (^{99m}Tc) bone scintigraphy, stress fractures appear as hyperaccumulation areas very similar to neoplastic lesions. In some cases, however, it is possible to observe some medical aspects which allow a more specific diagnosis; for example, the typical H-shaped or butterfly pattern of uptake in the sacrum is diagnostic of insufficiency fracture.

4.2.3 Computed Tomography

Computed tomography (CT) shows fractures as hypodense areas surrounded by a sclerotic area of variable level, depending on the age of the lesion, not associated with extra bone masses.

Its higher spatial resolution makes CT a more sensitive technique, compared to traditional radiology, in the identification of insufficiency fractures. The possibility of 3D reconstruction and elaboration is useful in case of fractures that run parallel to the axial scan plane, because these lesions may be undetectable otherwise. In addition, 3D reconstructions could suggest further information to the clinician about possible surgical and interventional therapies. Some skeletal segments, such as the sacrum and tarsus, are hardly visible on traditional radiographic representation, and therefore CT plays a crucial role in the examination of such regions.

4.2.4 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is as sensitive as bone scintigraphy to stress fractures, but far more specific, especially when complemented with the other techniques. The main advantage of MRI is the possibility to detect very early the intraspongious edema associated with recent fractures, which is hyperintense on T2-weighted images and even clearer on STIR (short-time inversion recovery) and fat saturation sequences that suppress hyperintense fat. The signal of the edema associated with a fracture is no different from the signal associated with other causes or with the hyperintensity associated with neoproliferative processes;

nonetheless, the fractures show a rather typical aspect. On T1-weighted images, they appear as hypointense areas surrounded by a hypointense rim, while on T2-weighted images, they appear as hypointense lines surrounded by hyperintense edema. The edema can be observed only during the acute phase and for a few months, and then its signal disappears, indicating that the fracture is rather old. The fracture line is not always evident, especially in cases of vertebral fractures; it is for that reason necessary to complement information from this method with data from the lesion site, especially for the differential diagnosis of pathological fractures. Contrast agent is not always necessary, but it can be useful in difficult cases, as it allows better definition of the fracture line, which remains hypointense with respect to the surrounding marrow. With pathological fractures, the contrast agent is useful to define the mass responsible for the lesion (Cuenod et al. 1996).

4.3 Fracture Sites

The vertebral body is the main site for insufficiency fractures. Changes in the vertebral bodies, when affected by osteoporosis or other pathologies that impair the elasticity of the bone, often show a progressive trend. In some cases, the fractures occur as a result of trauma (acute lesions) and are subordinated to the burden on the reduced trabeculae which are distributed in the vertebral body along the major stress lines. Shape deformation is the most typical alteration of a vertebral body with reduced elastic resistance, regardless of the cause (Cammisa et al. 1991).

At first, it is a microfracture consequence, and therefore these lesions have to be considered real vertebral fractures even without any discontinuity line on the bone. However, progressive osteopenia gives rise to fracture lines detectable through radiological investigation, which appear spontaneously or after moderate trauma. Dorsal and lumbar vertebrae and, in particular, the bodies located at the point of maximum axial load, the thoracolumbar junction (D12-T1), are the most affected. Both the classification and the nomenclature of the different forms of vertebral alterations are different and often in contrast.

Monoconcave or biconcave vertebral deformations, known as “fish vertebrae,” are an exaggeration of the normal concavity of the superior and inferior surfaces of the vertebral bodies, caused by a depression of both the superior and inferior vertebral end plates, with a consequent reduction of the central portion. In less severe cases, both anterior and posterior sides seem to be normally shaped, while in severe cases the body is totally flattened (Cammisa et al. 1991). There is no agreement among researchers about this deformation: not every case of biconcave alteration is defined as a fracture. Recent studies have defined biconcave fracture as a vertebral body height that is 15 % or 4 mm lower than the posterior height.

Beyond osteoporosis, biconcave vertebral deformation can be observed in osteopenia. In osteomalacia, for instance, the deformation is symmetrical, while in osteoporosis the same degree of deformation in both superior and inferior end plates is rather rare.

Wedge-shaped vertebrae (Fig. 4.1) are characterized by a loss of anterior vertebral body height without impairment of the posterior half. To correctly diagnose a wedge-shaped vertebra, the anterior vertebral body should be more than 15–25 % or 4 mm higher than the posterior side, because small congenital dysmorphisms are not uncommon. This frequently affects the thoracic portion, especially D6 and D7: in this site, the vectors of the load forces concentrate on the anterior side of the vertebra. The posterior column is rarely involved but has to be carefully evaluated because it could indicate a fracture instability. According to a model proposed by Denis, a posterior column lesion is unavoidably associated with instability. When the vertebra shows a more than 15 % reduction in height, the lesion is defined as a compression fracture, which at its worst is known as a flattened vertebra and involves the whole vertebral surface, which appears highly reduced in its size. When diagnosed, it is always necessary to suspect a pathological fracture, in particular due to multiple myeloma. Cammisa et al. (1991) developed a

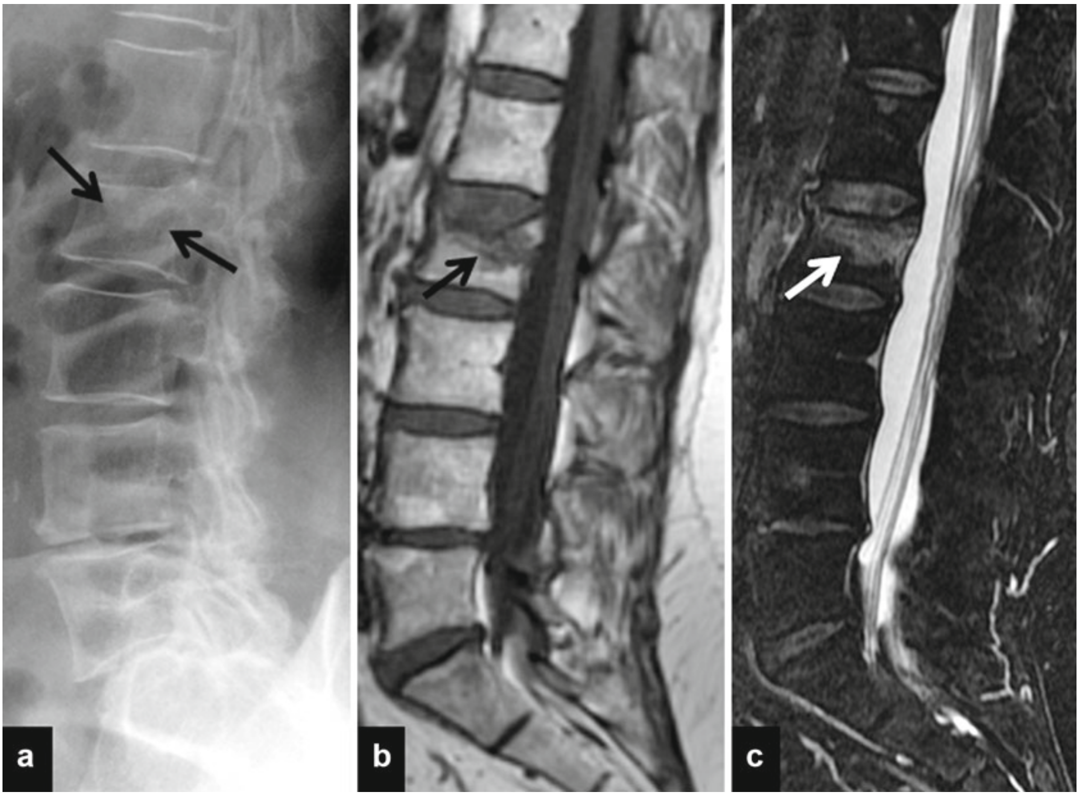

Fig. 4.1 Vertebral fractures in osteoporotic patients. (**a**) X-ray examination shows the deformation of the vertebral body, with a reduction in height of the front wall. It is also possible to identify the fracture indicated by *two black arrows*. (**b**) Sagittal T1-weighted image shows the fracture as a hypointense line (*black arrow*). (**c**) T2-weighted fat-saturated image shows the fracture line (*white arrow*) surrounded by intense edema

different classification of the collapsed vertebrae which shows a good correlation between the morphological pattern and the probability of malignancy. They distinguished four types of collapse: focal concave, diffuse concave, focal with an acute angle, and diffuse with an acute angle. Focal concave collapse is typical of benign lesions, and diffuse collapse with an acute angle is typical of malignant lesions, while the other two types have no known predictive value.

Traditional radiology is usually sufficient to diagnose and characterize vertebral deformations. Alterations of the trabecular texture can be identified when the mineral component is reduced by 30–40 %. Initially, the cortical structure is increased, in part due to its later resorption compared to the spongious part and in part because the vertebral end plates tend to undergo reactive sclerosis. The earlier resorption of horizontal trabeculae explains the more marked pattern of vertical trabeculae, which appear as radiopaque bands.

In later stages, the trabecular structure can become completely radiotransparent, causing the typical picture-frame aspect. Radiology can help to distinguish between metabolism-related and traumatic crush injuries: a break in the cortical component, with eventual mesh-related phenomena, suggests a post-traumatic lesion.

Traditional radiology is not the only source of qualitative information about the vertebral status; indeed, vertebral radiological or morphometric absorptiometry can overcome some of the limits of radiology by assessing objective parameters. The analysis measures the vertebral height at the level of anterior, center, and posterior walls. The analysis also calculates vertebral height ratios; a diagnosis of fracture is suggested by a reduction of a vertebral height beyond a certain threshold. This allows identification of small fractures that are asymptomatic most of the time and provides an advantage for the patient, as it may suggest therapy to prevent further and more severe deformations. According to current regulations, use of alendronate and other drugs provided by the Italian National Health System is allowed only in ascertained fracture cases.

CT is also a useful source of information when analyzing vertebral fractures. It is possible to recognize in the vertebral body sclerotic, lytic, and mixed alterations. Interruption of the cortical bone is well detected by means of CT multiplanar reconstruction (Cammisa et al. 1991).

CT is more accurate than traditional radiology for determining the age of a vertebral collapse, an important issue in treatment, as it allows some correlation of the lesion to the reported symptoms. The key elements are both the patient's medical history and the sclerotic component of the collapsed vertebral body, which is a reactive response after a fracture as an effort to heal and to give the vertebra more stability.

MRI has a key role in integrated diagnostic imaging of pathological, usually metastatic, fractures. Metastases can spread to any of the vertebrae, although the dorsal vertebrae are most affected, while osteoporosis fractures show typical sites and are rare above D7. While insufficiency fractures are limited to the vertebral body, pathological fractures often affect pedicles: it is possible to investigate this aspect by radiography, CT, or MRI. In the anteroposterior projection, as well as the coronal projection, the metastatic vertebra can appear deformed on a single side, which is another distinctive feature; moreover, another feature typical of the neoplasia is the intraosseous mass associated with the fracture.

MRI, although less accurate than CT in bone observation, allows analysis of the bone signal, which is of highly important diagnostic value. On T1-weighted images, recent insufficiency fractures usually show a horizontal band-like low signal intensity under the upper end plate; in contrast, during the chronic phase, the signal tends to become isointense with respect to other vertebrae with, occasionally, a thin hypointense band. Pathological fractures are usually homogeneously hypointense when the bone marrow is totally replaced, while in cases of focal marrow replacement, it is possible to observe a particularly intense contrast between tumor hypointensity and bone marrow high signal.

On T2-weighted images, insufficiency fractures are hyperintense during the acute phase, because of the edema, and then become isointense after 1–3 months. Metastases are hyperintense on T2-weighted sequences, even though densifying bone metastases can show a low signal. Fat suppression sequences, STIR and SPIR (selective partial inversion recovery), are very useful because the insufficiency collapse signal is analogous to other vertebrae signals, while metastases appear highly hyperintense. Contrast enhancement is rarely useful, as the pathological fractures absorb the contrast agent in a marked and nonhomogeneous way.

In the last few years, radiology has assumed a key role in vertebral insufficiency fracture therapy due to the development of percutaneous vertebroplasty, a minimally invasive technique based on CT and fluoroscopy image-guided stabilization of a vertebra by injecting a medical grade cement into the painful fractured vertebral body. Both the pain relief and the increased mobility seem to be encouraging, with an improvement in more than 80 % patients, when well selected, and a low complication rate (Anselmetti et al. 2004).

Femoral neck fractures are common among older people affected by osteoporosis: they are sometimes secondary to metastases, Paget disease, or they can be overload fractures among athletes. In subjects with osteoporosis, these fractures often follow a mild trauma and are a severe complication because of the associated high morbidity and mortality.

Intracapsular fractures can be divided, according to the Garden classification, into four types: stable fracture with impaction in valgus, complete but nondisplaced, complete and partially displaced, and fully displaced. Often they are complicated by avascular necrosis, pseudoarthrosis, and secondary arthrosis. Intertrochanteric

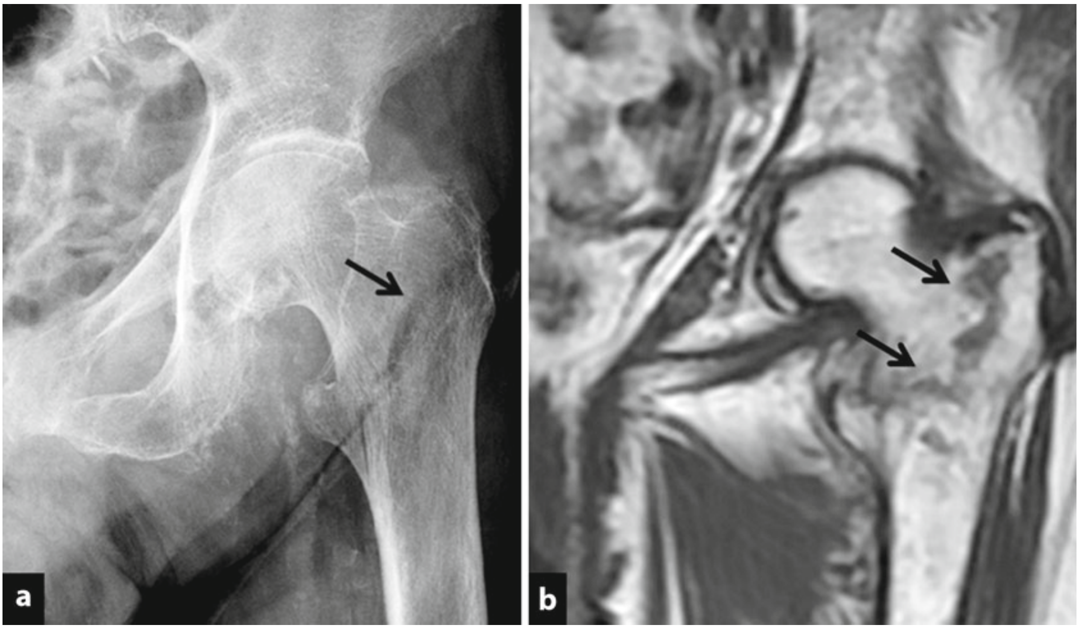

Fig. 4.2 Femoral neck fracture. (**a**) Radiographs clearly show the fracture line (*black arrow*). (**b**) Coronal T1-weighted image shows the fracture as a hypointense line (*two black arrows*)

fractures, often broken and associated with instability, are typically the result of a fall.

Traditional radiological diagnosis may be insufficient in the initial phases, as in other stress fractures; however, both scintigraphy and MRI are highly sensitive techniques that can be used in early stages (Fig. 4.2). STIR sequences are particularly useful, as hyperintense edema provides support for both the diagnosis and the follow-up. Indeed, the hyperintensity normally disappears within 6 months, whereas persistence of hyperintense signals suggests a repetition of trauma.

MRI is a reference technique in the analysis of subchondral femoral head insufficiency fractures, which may remain undiagnosed or be confused with osteonecrosis, thus leading to a rapid and severe decline of the articular function. The lesions appear as thin subchondral hypointense bands in T1- and T2-weighted images, in association with edema (Davies et al. 2004; Otte et al. 1997).

Parasymphyseal insufficiency fractures are not frequent but trigger serious diagnostic issues in the initial phases, as radiography may fail to identify the lesions, yet a linear vertical fracture may sometimes be observed. In the chronic phase, repair of these fractures may be recognized through the presence of exuberant sclerosis associated with irregular osteolysis, sometimes with a moth-eaten appearance.

The possibility of primitive neoformations can be excluded through the integration of CT and MRI; in particular, observation of a hyperintense mass in T2-weighted images with a thin hypointense edge is frequent and typical, with this edge undergoing enhancement after contrast enhancement.

Sacral insufficiency fractures are common in old people with osteoporosis or a history of recently irradiated pelvic tumors. Fatigue forms are more rare and occur in young and active individuals. Most of the time, fractures are bilateral (Fig. 4.3), have a vertical course which makes them hardly detectable through conventional radiography, and exhibit a typical butterfly pattern. Scintigraphy can be positive even in early phases, by showing the pathognomonic H-sign. In these forms, MRI can be an irreplaceable tool (Brahme et al. 1990).

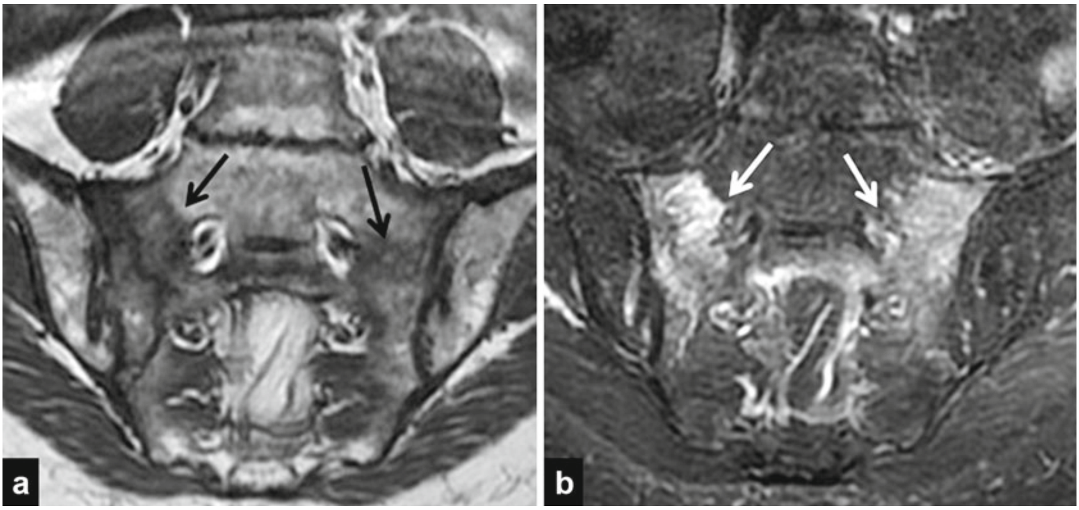

Fig. 4.3 Bilateral fracture of the sacrum. (**a**) T1-weighted image shows the fracture as a hypointense line (*black arrows*). (**b**) T2-weighted fat-saturated image shows the fracture line surrounded by intense edema (*white arrows*)

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