

● PERSPECTIVES

The clinical rehabilitation of spine and spinal cord disorders: detection and evaluation using SPECT/CT

Spine-related disorders are caused by several factors including (1) spinal nerve/visceral nerve stimulation by perivertebral aseptic inflammation, (2) spinal nerve/visceral nerve compression by injured perivertebral soft tissue, dislocated perivertebral small joint, and proliferative/degenerative tissue and, (3) secondary damage to the spinal cord, peripheral nerve, vessels and autonomic nerve, which further stimulate nerve root sheath and surrounding pain-carrying nerve fibers. In many cases, the source of pain cannot be detected by standard image modalities. Particularly in anatomically complex regions like the spine, SPECT/CT can be helpful for some aspects by introducing a metabolic dimension to the classical way of morphology-based diagnostic. The aim of the present review was to give an overview of the adoption of SPECT/CT in a clinical spine-focused setting.

Introduction

Beside degenerative alterations, fractures of the spine are a common cause of pain. Despite their small incidence they are of great importance due to potentially severe consequences even in those cases with no involvement of the spinal cord. Therefore, both degenerative alterations as well as fractures are an important field of work within orthopaedic surgery and traumatology.

In order to reduce associated morbidity and mortality, a timely therapeutic intervention is necessary. Therefore, a sufficient diagnostic work-up is essential.

However, with standard image modalities, some fractures, especially those of the Pars intra articularis or occult fractures of the vertebral body can often not be detected. Furthermore, origin of back pain in cases of degenerative diseases is diagnosable in only about ten percent by the current imaging techniques (Janssen et al., 2011).

Within these techniques, myelography, plain radiography, computed tomography (CT), and magnetic resonance imaging (MRI) have to be mentioned. Newer imaging modalities are single-photon emissions computer tomography (SPECT) and hybrid imaging techniques like SPECT/CT. Latter combines the highly sensitive but non-specific SPECT with very specific but less sensitive CT (Gregory et al., 2004; Groves et al., 2004; Van der Wall and Fogelman, 2007; Hirschmann et al., 2010). Thus, identification of potential pain foci is mentioned to be as high as 92% in the cervical spine and 86% in the lumbar spine (Matar et al., 2013). For this reason, SPECT/CT is considered to be a valuable diagnostic addition. The aim of the present review was to give a short overview of the adoption of SPECT/CT in a clinical setting.

Traumatic spinal injuries

The estimated incidence of spinal fractures in literature is around 64 per 100,000 persons. In young patients, they usually occur in the presence of a substantial external force, whereas in elderly they can be the result of simple falls and represent the most common first manifestation of osteoporosis. Consequences are often underestimated, especially in those cases with no involvement of the spinal cord. However, mortality rates in elderly after an osteoporotic spinal fracture are comparable to those after femoral neck fractures (Cauley JA et al., 2000). Thus, sufficient diagnostic work-up is essential in order to initiate a timely therapeutic intervention.

In this process, nuclear medicine imaging technologies today still play a minor role in general. Usually, most of the fractures might be diagnosed by means of a conventional X-ray or CT. However, several studies in the past have demonstrated advantages of planar scintigraphy, especially when searching for occult fractures and subtle lesions (Spitz et al., 1992; Heinrich et al., 1994). In these affected regions, bone metabolism is locally increased and perifocal hematoma, necrosis, as well as calcification may occur. The resulting phosphate complex then bonds with the Tc-99m-methylen-diphosphate, which is utilized in SPECT (Love et al., 2003; Palestro et al., 2009).

Other neglected lesions by conventional imaging techniques are traumatic spondylolysis. These lesions occur on the basis of fractured pars inter articularis of the vertebral body and are believed to be caused by an axial loading injury to the lumbar spine in hyperextension. Due to the anatomical localization, they are frequently not visible on conventional radiographs or CT scans

(Hession and Butt, 1996; Sairyo et al., 2006; Zukotynski et al., 2010). Due to the increased metabolic turnover of the affected region, sensitivity and specificity of SPECT is superior even partly to magnetic resonance imaging (Zukotynski et al., 2010). In combination with computed tomography, the lesions can readily be anatomically localized by SPECT/CT (Standaert and Herring, 2007; Zukotynski et al., 2010). Beside these acute traumatic injuries, stress fractures of the vertebral body occur with an incidence of around 6% and are normally located in the fourth or fifth lumbar vertebra (Van der Wall et al., 2007). They are the result of repetitive stress leading to an imbalance of continuous bone resorption and formation. Especially young athletic patients are affected, whereby they complain about an acute onset of pain (Kainberger et al., 2006). Using CT, these fractures are missed in up to 15% of cases, whereas they are visible in SPECT/CT due to increased local bone uptake caused by increased osteoblast activity (Roub et al., 1979; Congeni et al., 1997).

In patients with normal bone turnover, the sensitivity for the detection of a fresh fracture using SPECT/CT is within the first 48 hours around 95% and after 72 hours 100% (Holder et al., 1990; Lee and Worsley, 2006). In elderly patients, time to initial fracture detection may be increased up to one week. Within 6–9 months, the visualized bone uptake continuously decreases as bone healing progresses (Martin, 1983), but may be visible up to three years following a fracture.

Due to the steady decrease of tracer uptake, SPECT/CT is of great interest in evaluation about fractures age. Particularly in cases of multiple spine deformities, such as compression fractures in elderly patients, this is of great interest to distinguish between fresh and old lesions. Besides the resulting diagnostic benefit, the information is of great importance to choose the right treatment. Especially the quality of percutaneous kyphoplasty depends on the selective use of this modality in patients with acute (> 6 weeks old) or sub-acute fractures (> 3 months old) because suboptimal outcome has been reported in patients with chronic fractures (Crandall et al., 2004; Buchbinder et al., 2009; Kallmes et al., 2009). To secure this, SPECT/CT is a helpful alternative compared to MRI, especially in patients where MRI is not practicable *e.g.*, patient having pain while prolonged lying or due to motion artefacts which lead to inconclusive results.

Furthermore, SPECT/CT allows an accurate differentiation between malignant and benign compression fractures (Tokuda et al., 2011).

Degenerative spinal diseases

Osteoarthritis is one of the most common articular afflictions and can affect every joint. In the spine, degenerative diseases occur within the cartilaginous joints, the uncovertebral joints, synovial joints and the fibrous joints.

Radiography, CT and MRI imaging may reveal signs of degeneration in patients with low back pain including disc space narrowing, vacuum phenomena, sclerotic vertebral margin, osteophysis, eburnation, perivertebral calcification and spinal stenosis due to disc degeneration or facet joint cysts. However, similar findings may be partly observed in asymptomatic patient, too. Thus, the relationship between imaging finding and clinical symptoms remains unclear to a certain extent. In contrast to mentioned imaging modalities SPECT/CT visualizes the morphologic changes as well as metabolic activities of osseous lesions. Due to the precise localisation of the increased tracer uptake conclusions can be drawn which lead to the source of suffered pain.

Most affected locations are the facet joints of the lumbar spine (Carstensen et al., 2011). Diagnosis is not always clear because osteoarthritis of these structures is commonly seen on radiographs in symptomatic as well as in asymptomatic individuals. Furthermore, other diseases like post-discectomy syndrome, spondylolisthesis or segmental instability can be associated with facet joint arthrosis as well. Using SPECT/CT, the affected facet joint can be visualised by increased tracer uptake (Matar et al., 2013). With this information the right therapy can be chosen *e.g.*, targeted infiltration with corticosteroids and anaesthetics.

Degenerative changes of the discs can be visualized by signal changes within the functional unity of the disc and the cartilaginous endplate. Due to the degenerative alterations of the disc the mechanical (over) load increases within the endplate. As a result subchondral sclerosis and exophytic outgrowth as a sign of intervertebral osteochondrosis occur. In many cases degenerative changes appear at different location and extreme spinal osteophytosis is in great contrast to clinical symptoms. In these cases increased tracer uptake helps to differentiate between affected functional units (Figure 1). Due to the simultaneously conducted CT scan morphological information can be obtained to differentiate between degenerative changes and other skeletal abnormalities, in particular metastasis.

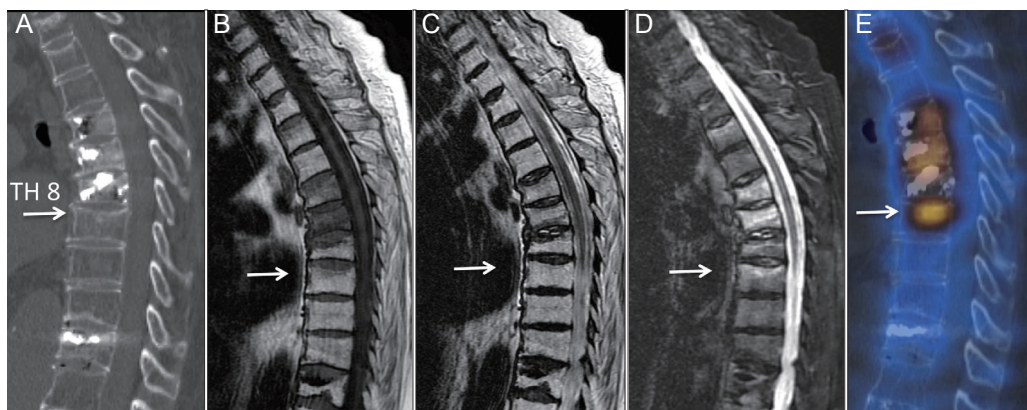


Figure 1 A 80 years old female with osteoporotic compression fracture of several vertebral bodies of the thoracic spine and lumbar spine (latter not shown). The MRI shows the fractures with kyphoplasty/vertebroplasty (B: T1-weighted, C: T2-weighted, D: short T1 inversion recovery). The CT and corresponding SPECT/CT (A and E) are showing the status post kyphoplasty/vertebroplasty. Note the elevated uptake in the cover plate of Thoracic segment 8 showing a fresh fracture.

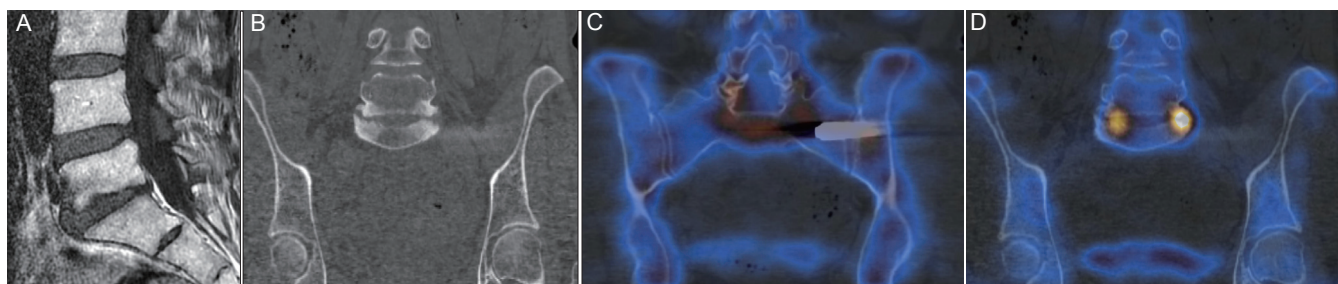


Figure 2 A 62 year old female patient with status post implantation of an “ifuse” rod for arthrodesis of the left iliosacral joint. The patient reported still pain several months after surgery – thus, there was suspicion for implant loosening/non-fusion or other pathologies. The MRI (A: T1-weighted) shows only minimal hypointense signal in L₅ and therefore no active osteoarthritis was reported. The CT (B) and SPECT/CT (C, D) show sclerotic changes in L₅ with elevated radionuclide uptake in this segment and an activated osteoarthritis was reported as the source of the pain. The implant of the left iliosacral joint is unremarkable (C).

Malignant spinal lesions

To assess the presence and extend of bone metastases bone scintigraphy using ^{99m}Tc-labelled diphosphonates has long been the mainstay investigation. It is extremely sensitive, which makes it useful for screening for early stage metastatic bone lesions in patients with malignant tumors (Schmidt et al., 2005). The main deficiency of planar bone scans is their relative lack of specificity (Minoves, 2003). Thus, it can be difficult to differentiate between metastases and other pathological findings such as degenerative diseases, infections, lack of fixation of metallic implants or benign bone tumors. Especially degenerative diseases often coexist in the cancer population due to in general older age. To clarify diagnosis, SPECT has been used to improve sensitivity (Kobayashi et al., 2005). In this context, certain patterns of tracer accumulation, like the focal uptake involving the vertebral body and the pedicles, have been shown to be more indicative for malignant diseases (Evan-Sapir et al., 1993). Further, the expansion of the lesion to the spinal canal with involvement or compression of the spinal cord is an ominous sign. Otherwise, increased uptake at the edge of the vertebral body adjacent to the disc or focal uptake in the facet joints without involvement of the pedicles is more characteristic for benign degenerative diseases (Evan-Sapir et al., 1993). However, the value of SPECT to exclude malignant involvement is controversial. Due to the additional anatomical imaging modality, SPECT/CT improves specificity compared with SPECT alone (Horger et al., 2004; Römer et al., 2006). In this context previous investigations by Horger and Bares demonstrated correct classification using SPECT/CT in over 85% of cases with equivocal foci, compared to 36% using SPECT alone.

Postoperative indications

Some patients report persistent pain following treatment of degenerative or traumatic afflictions of the spine with consecutive ilio-sacral arthrodesis or dorsal spine instrumentation and fusion. Due to persistent pain, previous investigations demonstrated the need of additional surgeries within four years after surgery to be as high as 14% (Martin et al., 2007).

Beside other questions to be answered by a chosen imaging technique, the assessment of implant loosening like pedicle screws is of great value in those patients with persistent pain following instrumentation. Usually the question is addressed to conventional X-rays or CT scans. Despite recent developments regarding new sequence modalities, MRI due to signal artefacts often leads to inconclusive results (Rutherford et al., 2007). In this context, SPECT/CT provides an alternative since alteration by metal artefacts is decreased (Lusins et

al., 1989; Larsen et al., 1996; Gates and McDonald, 1999) and loosening can be detected on the metabolic imaging component even if the CT is inconclusive based on metal artifacts.

Further pseudarthrosis after spinal fusion can be a cause of persistent pain, too. Usually, decrease of tracer uptake can be observed by SPECT/CT within the third postoperative month (Rager et al., 2012). In cases with consistently high uptake for more than a year after operation, non-union can be suspected (Gates and McDonald, 1999; Damgaard et al., 2010). Hereby previous investigations demonstrated that SPECT/CT seems to increase specificity for detection of non-union of interbody devices compared with CT scan alone (Rager et al., 2012). Especially to evaluate anterior fusion SPECT/CT seems to be superior (Rager et al., 2012).

After kyphoplasty or vertebroplasty, one of the most thoroughly documented complications are new vertebral compressions fractures of the adjacent segments (Uppin et al., 2003; Lin et al., 2004; Syed et al., 2005). Beside other risk factors like osteoporosis, prior vertebral fracture, cement leakage into the disk after treatment and older age the degree of height restoration of the cemented vertebrae increased the fracture risk of adjacent vertebrae (Kim et al., 2004). The following increased mechanical burden to the adjacent segments can be visualized by SPECT/CT (Figure 2). With this knowledge, a well-founded estimation can be made about the risk of adjacent fractures and whether a patient might profit from an additional preventive operation.

Further questions to be answered by SPECT/CT are instability of the instrumentation, low-grade infection and finally epi- or subfussional degeneration by evaluating increased uptake due to (erosive) osteochondrosis (Rager et al., 2012).

Infection

In patients with suspicion of local infection due to trauma or surgery, confirmation and determination of the exact location is of great interest. Using computed tomography or magnetic resonance imaging observed infection-related changes are normally very unspecific nature and usually evident only in late stages. Furthermore, implant associated artefacts may substantially deteriorate image quality. Compared to CT and MRI, SPECT/CT allows the detection of an infection despite metal artefacts in the CT-component and the exact localization by visualising cortical destructions, foreign bodies, or sequestrums. Due to the detailed anatomical correlation it is furthermore helpful to differentiate between osteomyelitis and soft tissue infections (Bar-Shalom et al., 2006). Therefore, it plays an important role in the detection of implant-associated infections (Navalkissoor et al., 2013). To secure



this and to improve sensitivity and specificity a combination between Dicarboxypropandiphosphonat (DPD) scintigraphy with radioactively marked leucocytes is recommended (Navalkisoor et al., 2013). In Europe, anti-granulocyte scintigraphy is more popular and has been proven equal in value (Richter et al., 2011). However, it must be mentioned that sensitivity and specificity vary depending on the body region. In the area of the spine FDG-PET/CT is currently the standard imaging modality and superior to SPECT/CT. Latter is used when detecting an infection of an extremity (Stumpe et al., 2002; Linke et al., 2010).

Conclusion

Beside the common imaging modalities, SPECT/CT has proved to be very helpful in clinical routine by introducing a physiological dimension to our classical way of morphology based diagnostic. However, applicability for spinal cord pathologies is rare, it is of great interest in anatomically complex regions such as the spine to evaluate the enclosing structures of the spinal cord.

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