Chapter 9

Summary

This thesis describes the clinical use of a new infection tracer namely $^{111}$In-Biotin for the diagnosis of vertebral infection.

**Chapter 1** is an overview on vertebral infection and its etiology. In this chapter all diagnostic methodologies clinically used, the diagnostic morphological imaging as MRI and nuclear medicine inflammation/infection tracers nowadays available ($^{67}$Ga, $^{18}$F-FDG, labelled leukocytes) are described. Advantages and limits of each modality are discussed as well as the researches performed in the last 13 years to obtain an infection tracers to overcome limitations of current available methodologies.

In **Chapter 2** the low specificity of labelled antibiotics used for the diagnosis of infection in animal models is discussed. Since their mechanism of action none of these agents is unable to bound exclusively to bacteria. Thus, their sensitivity and the specificity can differ according to type of infection, type of micro-organism, infection site and host clinical conditions/response. In this chapter the minimum number of bacteria that can be detected in vivo to provide bacterial imaging in clinical applications and the calculated number of labelled antibiotic molecules for bacteria, are presented. Results suggest that, the majority of radioactivity at site of infection is non-specifically bound to bacteria and it is due to presence of plasma leakage from capillaries. Moreover, some radiolabelled anti-microbial agents have also shown to bind to monocytes and granulocytes.

**Chapter 3** reports the results of a meta-analysis of published papers on bone infection. Bone infection is divided into three groups: peripheric post-traumatic and prosthetic joint infection, infections of the vertebral column and sternal wound infections. In the meta-analysis of peripheric post-traumatic and prosthetic joint infection publications 89 studies published between 1984 and 2004 have been analysed. Thirty papers on infections of the spine published between 1984 and 2004 have been evaluated and 11 original papers and two reviews (published from 1982 to 2004) on imaging of sternal wound infections with $^{67}$Ga, bone scintigraphy with $^{99m}$Tc-MDP, WBCs labelled with $^{111}$In oxine or $^{99m}$Tc-HMPAO and $^{99m}$Tc-MoAb anti-granulocyte were evaluated.

**Chapter 4** describes the first study of the avidin/$^{111}$Indium-biotin approach in patients with bone infections. This study was performed in patients with various
orthopaedic pathologies (intermediate suspected osteomyelitis of the trunk, infection/inflammation of prosthetic joint replacements and suspected osteomyelitis of appendicular bones). A comparison between Avidin/\(^{111}\text{In}\)-biotin scintigraphy and \(^{99m}\text{Tc}\)-HMPAO-labelled leukocyte scintigraphy is presented. The diagnostic performance of avidin/\(^{111}\text{In}\)-biotin scintigraphy in patients with prosthetic joint replacements or osteomyelitis of appendicular bones was similar to that of \(^{99m}\text{Tc}\)-HMPAO leukocyte scintigraphy, while the avidin/\(^{111}\text{In}\)-biotin approach clearly performed better than \(^{99m}\text{Tc}\)-HMPAO leukocyte scintigraphy in patients with suspected vertebral osteomyelitis. These results demonstrate the feasibility of the avidin/\(^{111}\text{In}\)-biotin approach for imaging sites of infection/inflammation in the clinical setting especially in the study of axial skeleton and the advantages in terms of practicability and biological risk of this new tracers instead of traditional procedures.

Streptavidin accumulates at sites of inflammation and infection as a result of increased capillary permeability. Beside its role as bacterial growth factor, biotin forms a stable and high affinity non-covalent complex with streptavidin. In Chapter 5 it is described the evaluation of the diagnostic performance of the two-step streptavidin/\(^{111}\text{In}\)-biotin imaging in patients with suspected vertebral osteomyelitis. Scintigraphic results are compared with radiological imaging (MRI and CT). Streptavidin/\(^{111}\text{In}\)-biotin scintigraphy is highly sensitive and specific for early detection of vertebral osteomyelitis and its accuracy is clearly higher than for either MRI or CT. Streptavidin/\(^{111}\text{In}\)-biotin scintigraphy is potentially very useful for guiding clinical decisions and appropriate therapy.

Chapter 6 describes the study of labelled Biotin as a growth factor used by many bacteria. This study evaluates the potential of \(^{111}\text{In}\)-Biotin scintigraphy to diagnose vertebral infections in patients with suspected hematogenous and postsurgical infections. The results showed that \(^{111}\text{In}\)-Biotin scintigraphy presents high diagnostic accuracy. This technique is easy to perform and requires short imaging time-point after the intravenous tracer injection. Moreover the relation of \(^{111}\text{In}\)-Biotin to bacteria proliferation rate of at site of infection is discussed and suggested as issue of further investigation.

Chapter 7 describes and establishes the add value of SPECT/CT acquisition of \(^{111}\text{In}\)-biotin scintigraphy for diagnosis of vertebral infection, moreover in differentiation between bone and soft paravertebral tissues involvement respect on planar and SPECT images. The results of the study showed a sensitivity of 93.8% and specificity of 94 % of \(^{111}\text{In}\)-biotin SPCT/CT scintigraphy respect on sensitivity and specificity of SPECT (90 % and 94 %) and planar images (sensitivity of 83 % and specificity of 72 %). \(^{111}\text{In}\)-Biotin SPECT/CT improves the diagnostic accuracy in comparison to planar images and SPECT acquisition scintigraphy. \(^{111}\text{In}\)-Biotin
SPECT/CT is able to differentiate between bone and/or soft tissues involvement of infection and it is a valid tool before choose a correct therapy in clinical setting. 

**Chapter 8** is a clinical update for practical guidelines in osteomyelitis. Bone infections represent a diagnostic or therapeutic challenge for the infectivologists, orthopaedics, radiologists and nuclear medicine physicians. Radiographs and bone cultures are mainstays for the diagnosis of bone infections but are often useless in the management of these patients. In diagnosing vertebral osteomyelitis, a series of haematochemical assessments must be carried out, including indices of inflammation, culture tests on biological liquids and instrumental examinations, including biopsies. Here the advices for diagnosis of skeletal infections are summarized. 

The advantages and limits of MRI and bone biopsy are also described. Nuclear medicine techniques offers for axial skeleton a combination of an inflammation agent (\(^{67}\)Ga-citrate) and a metabolic agent (\(^{99m}\)Tc-MDP) which together enable the diagnosis of vertebral infection. \(^{18}\)F-FDG PET, where available, has a significant impact for spine infections evaluation because of its high sensitivity, but at cost of a unsatisfactory specificity.