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Cardiac Rhythm Management Device Infections: Imaging Examinations to Direct Replacement Timing

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1. Introduction

In this paper we describe the management of ICD (implantable cardioverter defibrillator) carriers who undergo extraction of infected leads and who, in view of the need for same-side reimplantation, are studied with ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography with computed tomography (PET-CT) scan, or with leukocyte technetium-99m hexamethylpropylene amine oxime (^{99m}Tc-HMPAO) scan before reimplantation, in order to rule out a residual infection at the site of original implantation.

2. Case report 1

A 59-year-old man was admitted to our Institution with a three-week history of chills and fever (maximum 39.5°C). He had been implanted previously with a biventricular ICD placed at the left subclavicular region and had undergone repositioning of the right ventricular lead two months before the current hospitalization.
On admission, he had a high erythrocyte sedimentation rate (53 mm/h) and C-reactive protein (45 mg/L); blood cultures were positive for *Staphylococcus hominis* and transesophageal echocardiography visualized a vegetation on the right ventricular lead at the level of the tricuspid valve. Moreover, a chest ^{18}F-FDG PET-CT scan showed enhanced ^{18}F-FDG uptake at the left subclavicular region and along the intracardiac portion of the leads, thus supporting the diagnosis of device infection (figures 1 and 2). For that reason, intravenous antibiotics were started and the patient underwent successful transvenous lead extraction. The post-procedural course was free from complications, with no further evidence of systemic or local infection. After 14 days, an attempt to re-implant a new biventricular ICD from the contralateral side

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failed as selective angiography documented total occlusion of the right subclavian vein, whereas the left one was shown to be patent (figures 3 and 4).
At that point, in order to place the new biventricular ICD via the left subclavian vein, we referred the patient for a chest ^{18}F-FDG PET-CT. This showed focal enhanced ^{18}F-FDG uptake in the soft tissues at the left subclavicular region, supporting a diagnosis of residual local infection at the site of the original implantation (figure 5). We thus maintained the patient monitored in the Cardiology Ward, on combined intravenous and oral antibiotic therapy. After 15 more days we repeated a PET-CT scan, which showed normalization of ^{18}F-FDG uptake at the left subclavicular region, where we therefore decided to implant the new biventricular ICD via the left subclavian vein. The patient had no more infection-related symptoms or signs at 1, 3 6 and 12 month follow-up visits.

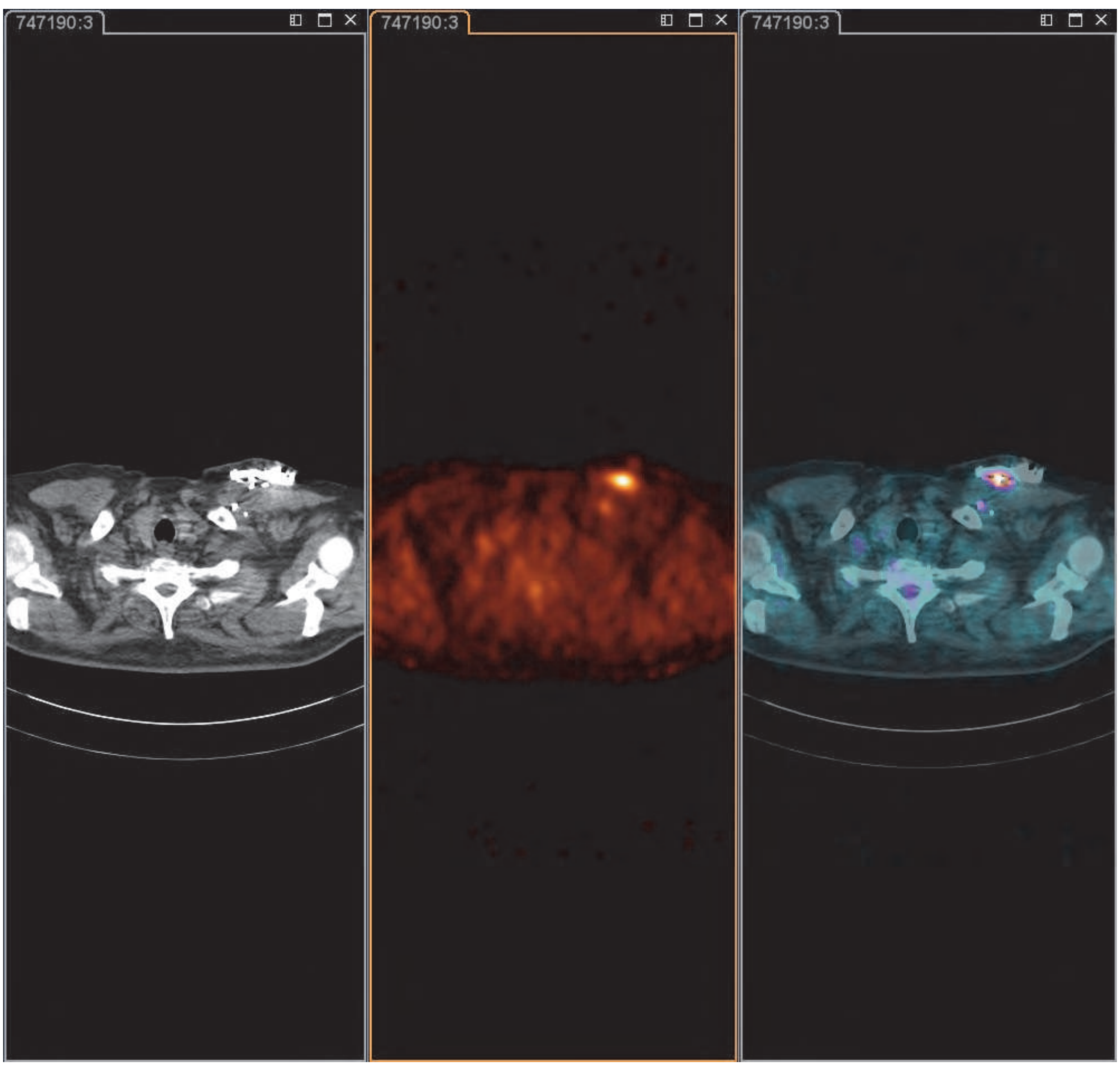

Fig. 1. Chest ^{18}F-FDG PET-CT showing enhanced 18F-FDG uptake within the ICD pocket. Left to right: CT image; PET image; PET-CT merge.

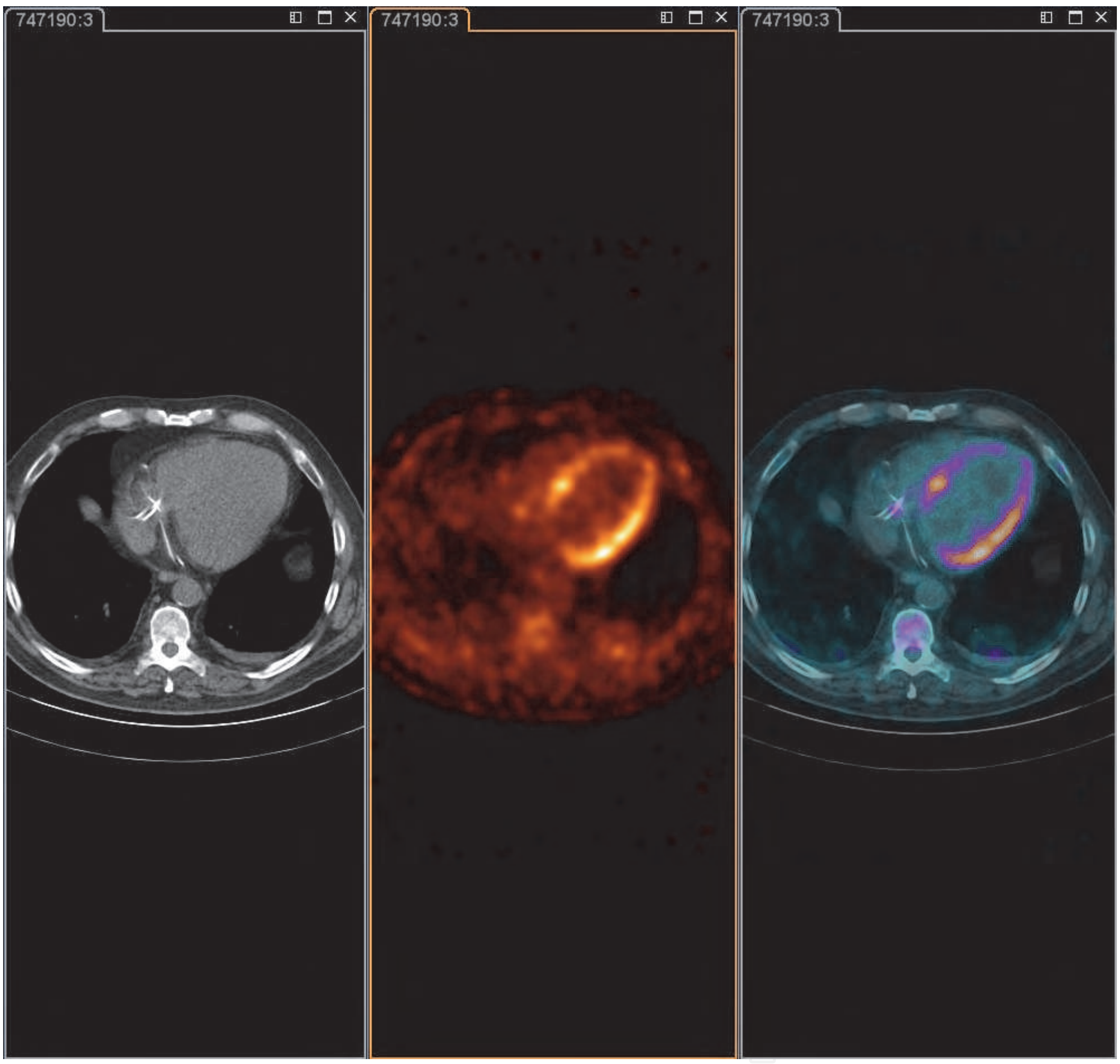

Fig. 2. Chest 18F-FDG PET-CT showing enhanced 18F-FDG uptake along the intracardiac portion of the right ventricular lead running across the tricuspid valve. Left to right: CT image; PET image; PET-CT merge.

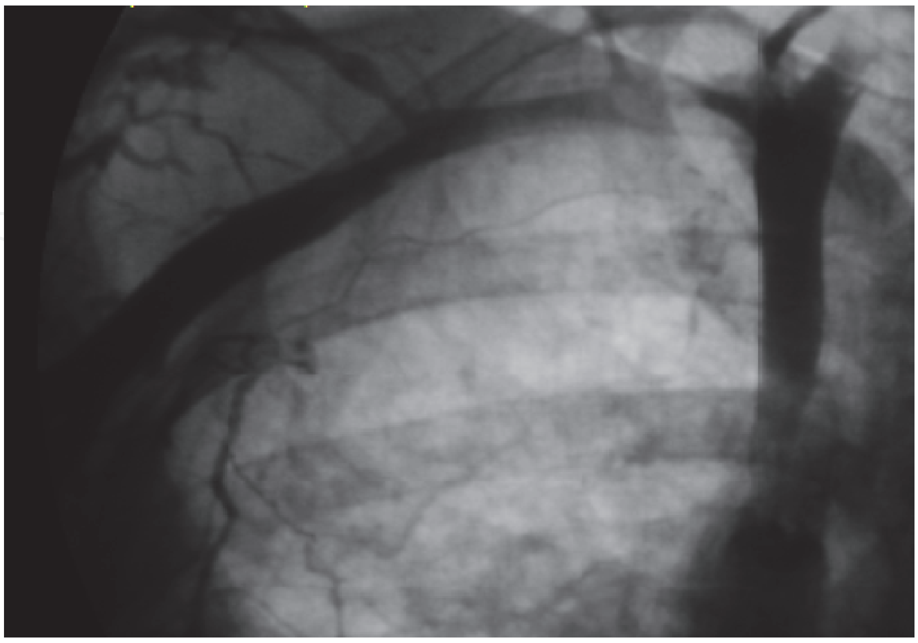

Fig. 3. Selective angiography of the right subclavian vein.

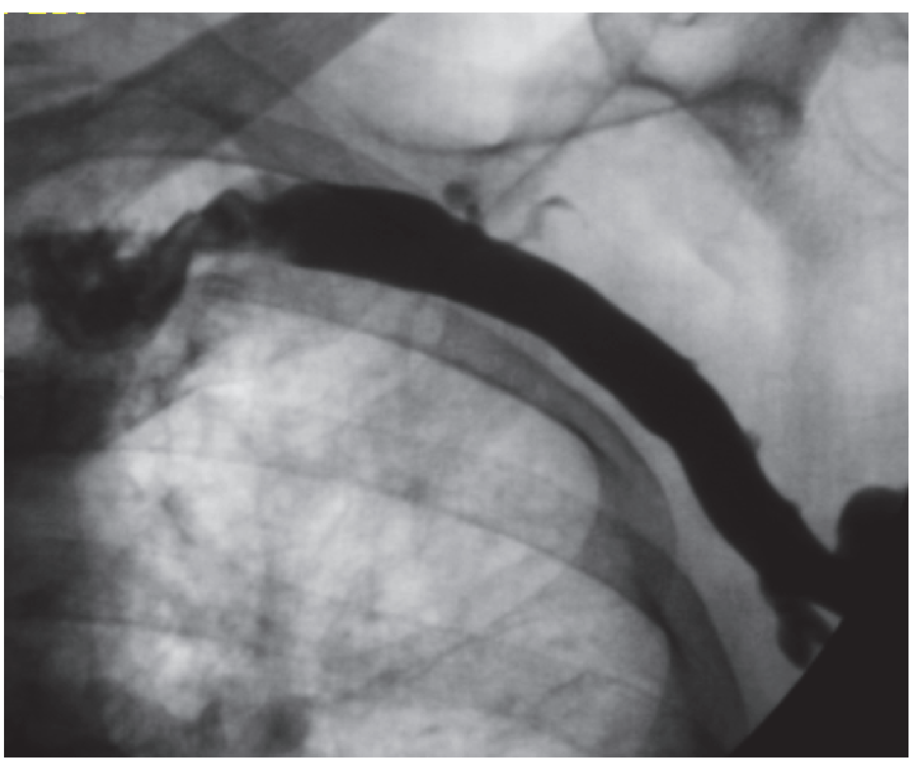

Fig. 4. Selective angiography of the left subclavian vein.

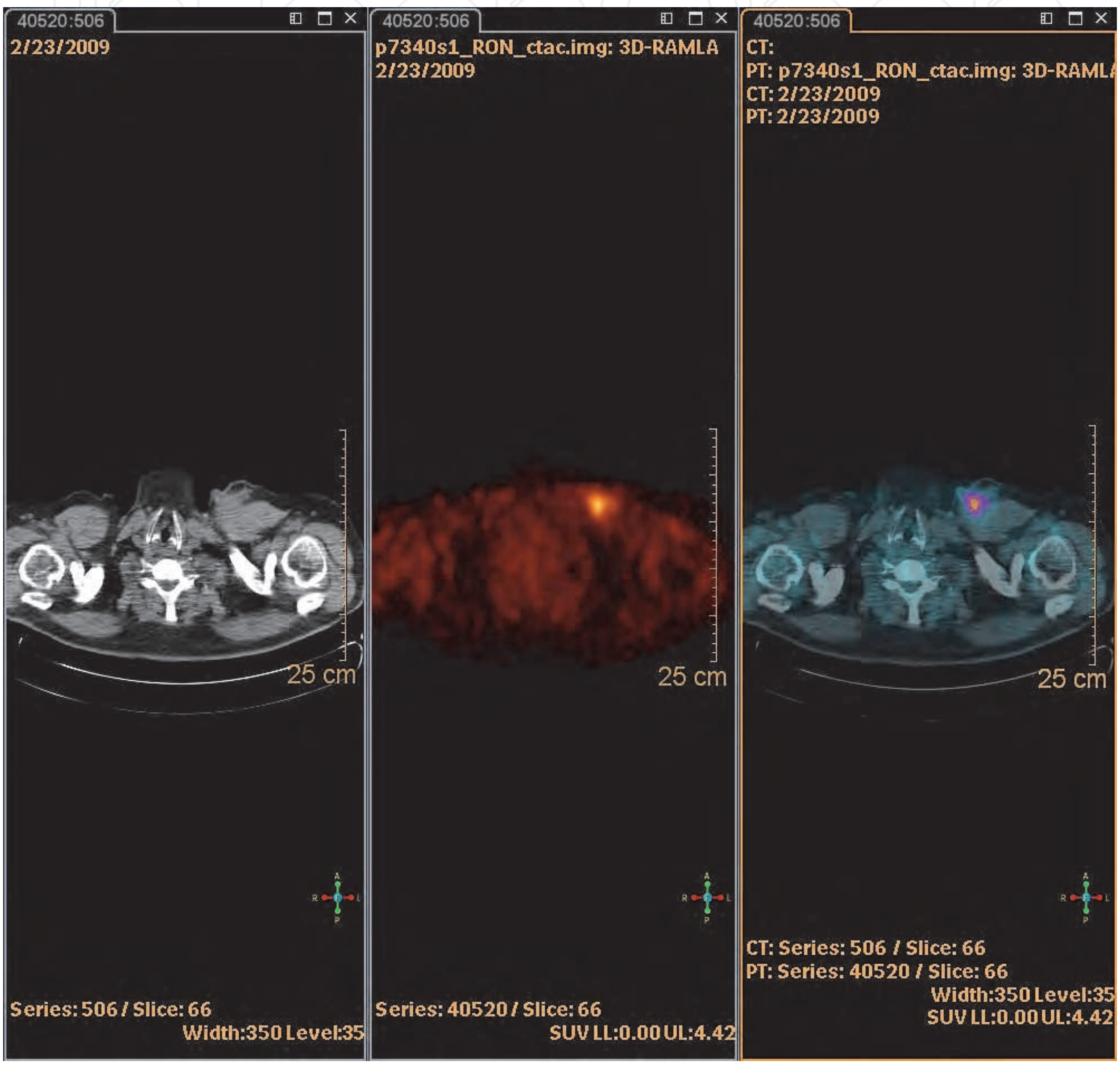

Fig. 5. Chest ^{18}F-FDG PET-CT showing focal 18F-FDG uptake in the subclavicular region after ICD extraction. Left to right: CT image; PET image; PET-CT merge.

3. Case report 2

A 71-year old man with two previous remote myocardial infarctions was admitted to our Institution for ICD lead extraction and reimplantation. He had undergone ablation of sustained ventricular tachycardia in 2000 and was implanted with a bicameral ICD at a left subclavicular site. When the generator was replaced in 2007, the device had become infected and both the generator and leads had to be extracted; the patient was then reimplanted on the right-sided subclavicular site. In April 2010, rising defibrillation impedance prompted a device revision procedure, which however led to a second device infection.
The patient came to our Institution with neither fever nor other symptoms and, after a transoesophageal echocardiogram excluded lead vegetations, he underwent extraction of both generator and leads without complications, followed by antibiotic therapy guided by sensitivity testing from the right-sided ICD pocket.
The issue of ICD reimplantation proved more difficult than initially thought, as the left subclavian vein, though seemingly patent on ultrasound and CT imaging, was shown by angiography to possess only a winding, thread-like residual patency with extensive collateral circulation (figure 6), whereas the right subclavian vein was shown to be fully patent. Therefore the possibility of using the previously infected right-sided subclavicular pocket was then taken into consideration and a ^{99m}Tc-HMPAO labelled leukocyte scan and SPECT was used to evaluate whether residual inflammation was present within the pocket (figure 7). The scan was negative and the new ICD was reimplanted at the right subclavicular site.

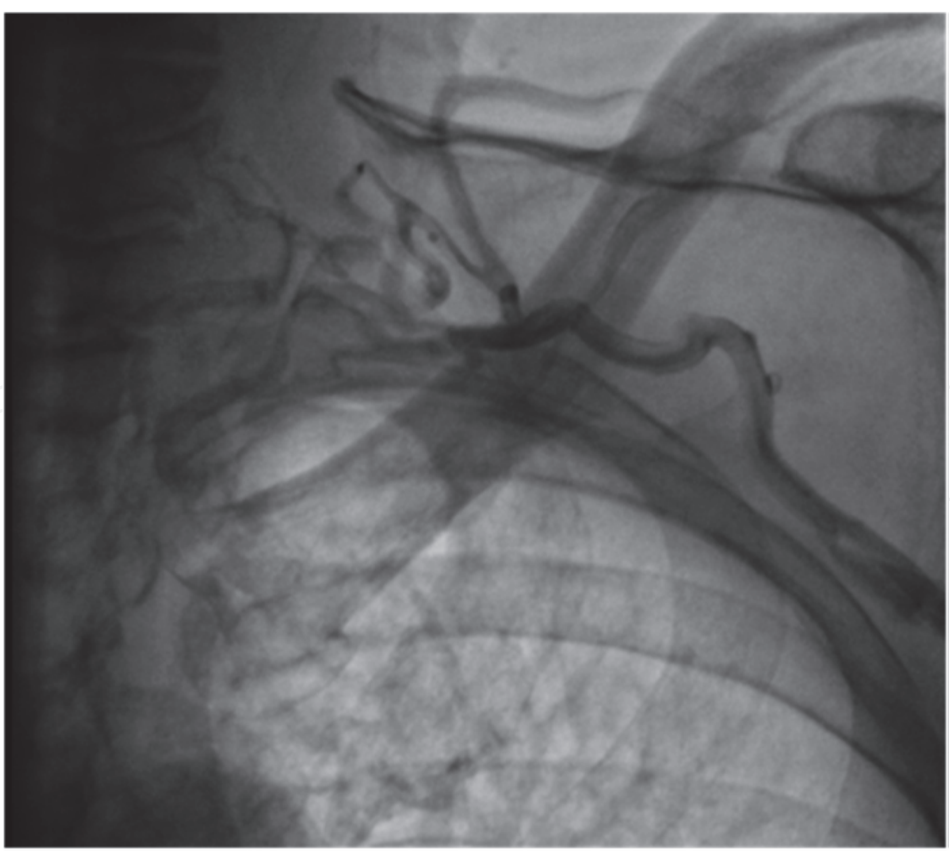

Fig. 6. Selective angiography of the left subclavian vein.

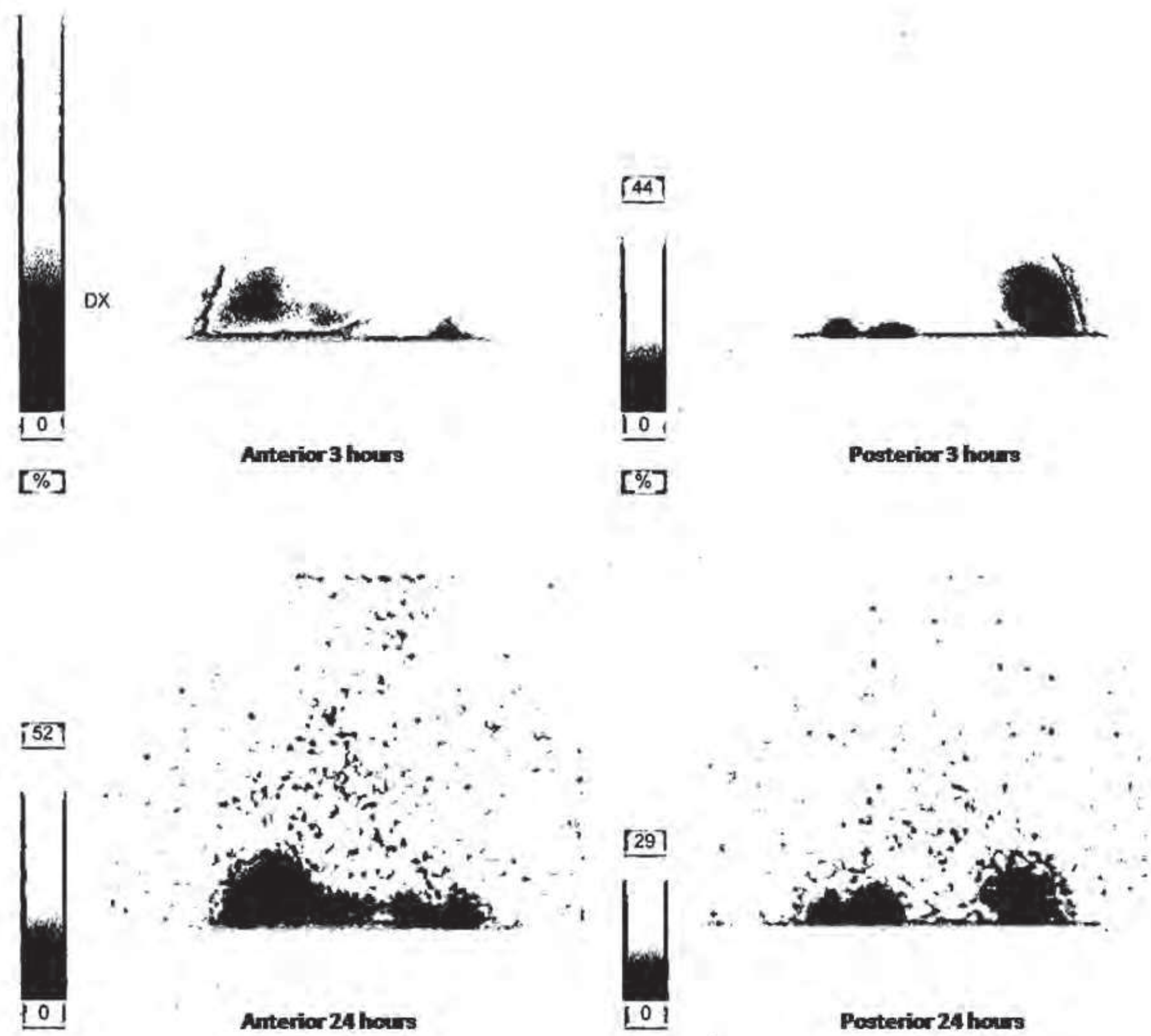

Fig. 7. White blood cell scintigraphy scan, showing no concentration of marked white blood cells at either subclavicular site.

4. Discussion

Generator or lead infection is the most common indication for removal of cardiovascular implantable electronic devices (CIED), and the increasing number of cardiac device implants explains the subsequent rise in the number of such procedures[1,2]. Recent guidelines provide detailed indications for lead extraction due to infection, depending on the involvement of such structures as heart valves, catheter leads, device pocket, or on the presence of sepsis/bacteremia; furthermore, directions about the timing of device reimplantation following infected device removal have been drawn up[3].

However, the authors just recommend not to place a second CIED in the same side as the extracted one and no specific indications have been established when same-side implantation is needed and an epicardial approach is not preferred. This might hold particular importance in patients who need prompt replacement of their device, for example because of stimulation-dependence or severe conduction disturbance.

To the purpose of safely implanting a CIED at the same site of the explanted one, an imaging investigation able to diagnose subclinical infection involving the subcutaneous soft tissues would be desirable. Few diagnostic tools have been specifically studied with the aim to detect residual infection at the sites of removed generator and leads, and the decision to reimplant is mainly based upon the absence of clinical signs or symptoms and on laboratory tests (mostly blood cultures) showing no sign of a local or systemic inflammatory/infectious process after a predetermined period of time[3].

FDG-PET and PET-CT scan have been used in the past decade in the diagnosis of patients with infection and inflammatory disorders, such as fever of unknown origin[4,5]. Combined FDG-PET and CT imaging has the potential to determine the sites of infection or inflammation with high precision, and it proved unaffected by significant metal-related artifacts due to CIED in phantom and patient studies (with an exception for ICD coils in one study)[6-8]. Possible limitations of this diagnostic technique are the spatial resolution (although our system achieves a 4 mm resolution after merging the two imaging modalities) and the possible occurrence of high-density material-related artifacts, which we avoided by comparing the combined images to the pre-acquired FDG-PET scan alone[9].

FDG-PET has been used in a previous report to detect a suspected pocket and lead infection and to opt for pacemaker removal in a patient with no other signs of infection detectable on clinical and instrumental examinations; in that case, PET scan showed a faint non-specific uptake in the empty pocket after pacemaker removal[10]. However, the ^{18}F-FDG uptake pattern can help to reliably distinguish between a healing scar-related signal and an infection-related one. In another published image, PET-CT was used to investigate a suspected foreign-body infectious endocarditis in a patient with an implanted ICD and a recent purulent discharge from the device pocket, that had been treated with antibiotics, and it detected an infection concerning both the wire line from the device up to the right atrium and the catheter within the coronary sinus[11].

Leukocyte ^{99m}Tc-HMPAO scan is also used for the visual diagnosis of infectious and inflammatory processes,[12-14] based on the principles that white blood cells concentrate in site of ongoing inflammation. The use of this technique is well-documented for the diagnosis of infection of endovascular prostheses such as grafts and stents[15-16] and of left ventricular assist devices[17], while there is scarcer evidence in CIED infections. Ramackers and colleagues reported in 1995 the use of ^{99m}Tc-HMPAO labelled granulocyte scan with SPECT imaging for the detection and follow-up of recurrent infective endocarditis in a patient equipped with a pacemaker.[18] In that case, the patient's conditions excluded the possibility of lead extraction, so the SPECT scan was used not only to diagnose the infection, but also to document disappearance of inflammation after adequate antibiotic therapy, despite no significant change on echocardiography. Howarth and colleagues reported in 1998 the use of ^{99m}Tc-HMPAO labeled leukocyte scan to demonstrate infection of pacing leads in a patient with a cardiac pacemaker.[19] In that case, initial gallium- and technetium-labeled leukocyte scans were negative, but repeat ^{99m}Tc-HMPAO scan after five weeks allowed to localize the septic focus, an infected thrombus along the pacing leads in the subclavian and brachiocephalic veins. Lead extraction was necessary before the patient's conditions could improve. A more recent publication used indium-111 leukocyte scan with SPECT for much the same purpose.[20]

We used the PET-CT scan and marked leukocytes scan after lead extraction to rule out a residual infection in the region of previous implantation, in order to feel safer in performing

such a procedure and to set the date for ICD reimplantation. While there is no evidence on the relative advantages of one over the other in CIED infections, the two techniques described in our case reports have been compared for the diagnosis of infection of an aortic graft in a single case report, in which it was observed that ^{18}F-FDG PET-CT was able to diagnose the infection, whereas ^{99m}Tc-HMPAO labelled leukocyte scan was not.[21]
Given the continuous advances in technology and the absence of other reliable diagnostic tests, this approach may prove to be the study of choice in the foreseeable future for precise localization of involved sites and as a tool to direct CIED replacement timing.

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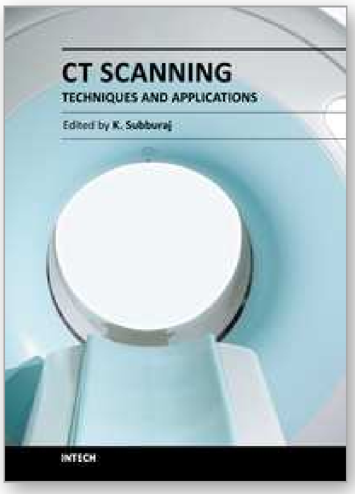

CT Scanning - Techniques and Applications

Edited by Dr. Karupppasamy Subburaj

ISBN 978-953-307-943-1
Hard cover, 348 pages
Publisher InTech
Published online 30, September, 2011
Published in print edition September, 2011

Since its introduction in 1972, X-ray computed tomography (CT) has evolved into an essential diagnostic imaging tool for a continually increasing variety of clinical applications. The goal of this book was not simply to summarize currently available CT imaging techniques but also to provide clinical perspectives, advances in hybrid technologies, new applications other than medicine and an outlook on future developments. Major experts in this growing field contributed to this book, which is geared to radiologists, orthopedic surgeons, engineers, and clinical and basic researchers. We believe that CT scanning is an effective and essential tools in treatment planning, basic understanding of physiology, and and tackling the ever-increasing challenge of diagnosis in our society.