^{18}F-FDG PET/CT for cardiac implantable electronic device infection

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There are many challenging infectious disease questions in diagnostic radiology where ^{18}F-FDG PET/CT may be a practical and useful solution.[1, 2] One of them is related specifically to infection of cardiac implantable electronic devices (CIED). There are an increasing number of CIED procedures accompanied by an even higher rate of increasing cases of infection, partially due to the aging of the new device recipients with multiple comorbidities and longer hospital stays.[3] Infection of a foreign body such as a CIED can quickly present a high risk of mortality, if not treated appropriately. There is an increasing need for diagnostic evaluation of a CIED which remains a challenge for current anatomical imaging modalities. For example, CT and MRI findings are non-specific for infection and are affected by metal artifacts. Transthoracic (TTE) or transesophageal (TEE) echocardiography is limited to evaluation of CIED lead related intra-cardiac vegetation, and not useful for the extra-cardiac portion of the lead and the device pocket.

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^{18}F-FDG PET/CT may provide added value in the evaluation of CIED infection in a clinically suspected case, and help to localize the site of infection, for example, whether there is an infectious process involving a CIED deep pocket, or if an infection is simply limited to the superficial tissues, which requires different management. A key advantage of ^{18}F-FDG PET/CT over anatomic imaging modalities is detecting infections early, before morphological changes ensue.[4] Areas of infection have increased glucose uptake due to increased expression of glucose transporter (GLUT) family isotypes among activated immune cells in areas of infection and bacteria's reliance on glycolysis as an energy source.[5] ^{18}F-FDG PET/CT offers similar to relatively higher sensitivity and specificity as other nuclear radiotracers used in infection such as WBC scan, with the additional benefits of safety/ease of use, lower radiation dose, and improved spatial resolution.[6] An added advantage of ^{18}F-FDG PET/CT is the ability to detect other potential sources of infection in a single study because it is a full body scan.

There are several important challenging management questions involving CIED where ^{18}F-FDG PET/CT can be particularly useful. Is the patient likely to respond to IV antibiotics? Will the CIED need to be replaced? Is there an infection along a lead? Is there another unknown source of infection somewhere else that is complicating the clinical picture?

Diagnostic interpretation

When evaluating CIEDs with ^{18}F-FDG PET/CT, there are three primary areas where close attention is

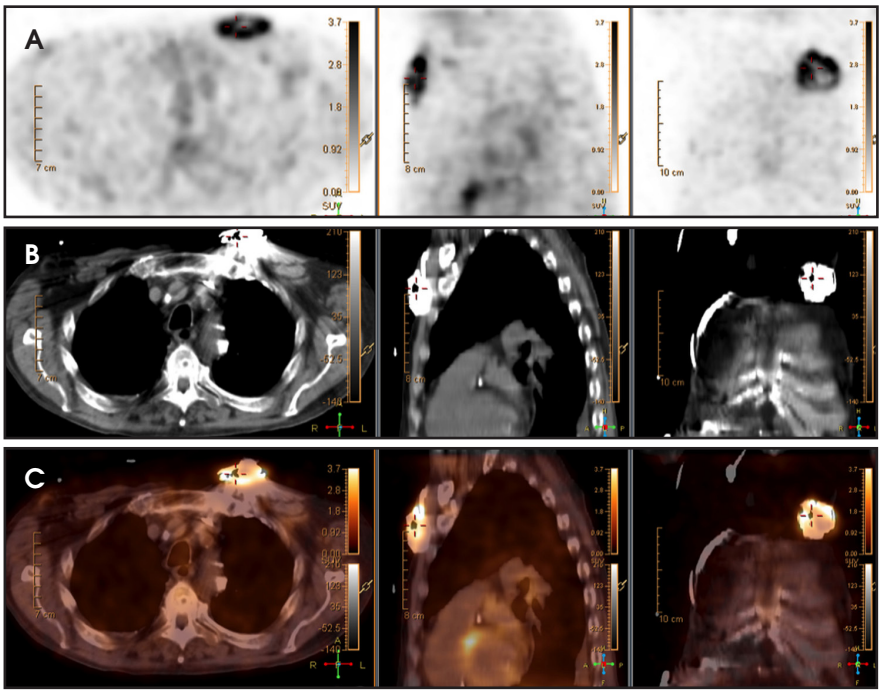

FIGURE 1. *An example of CIED pocket infection. There are several areas of focal increased ^{18}F-FDG uptake within the pocket of the CIED device in the left upper chest wall, many of which contact the device itself. This pattern of increased uptake is highly concerning for infection and should indicate device removal. Axial (left), sagittal (middle) and coronal (right) views of PET alone (A), CT (B) and fused PET/CT (C) images.*

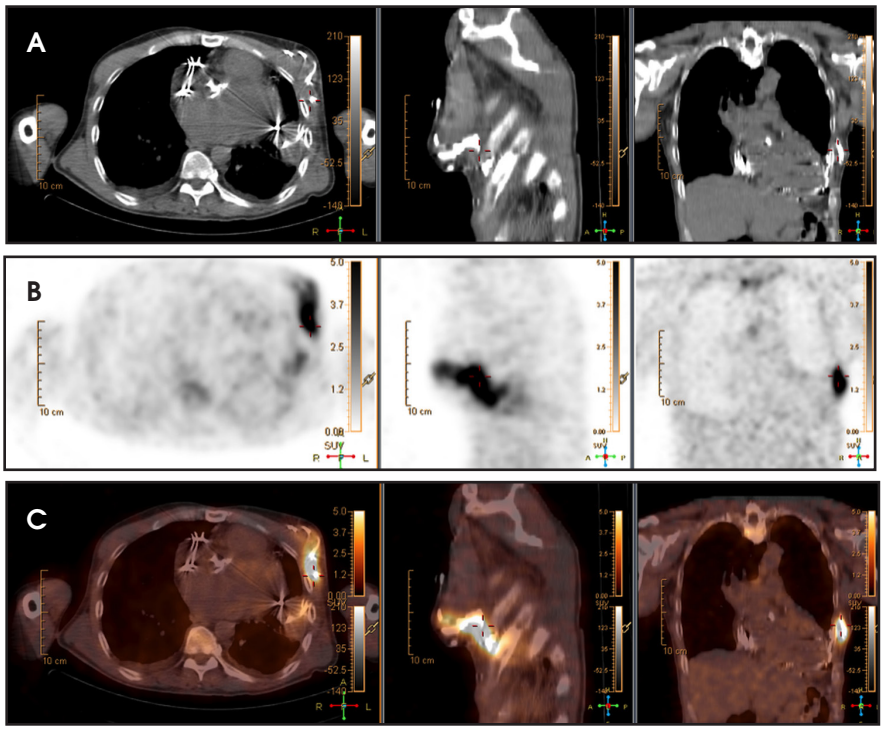

FIGURE 2. *An example of CIED lead infection. The series above demonstrates focal increased uptake on ^{18}F-FDG PET along the path of the lead in the left lateral chest wall. The findings are highly suspicious for infection and should prompt removal of both the device and the leads. Axial (left), sagittal (middle) and coronal (right) views of CT (A), PET alone (B), and fused PET/CT (C) images.*

necessary. It is important to evaluate the superficial tissues above the device in the chest wall, the device pocket, and the leads. If infection is limited to the superficial tissues, but not in contact with the device itself or the deep tissues, patients typically respond well to treatment for the superficial skin infection alone without the need for device removal. If infection is deeper or involves the device, then device removal is necessary (Figure 1).

Device lead infection can present a diagnostic challenge because it can often not be appreciated on the surface and is often not associated with anatomical imaging findings such as a fluid collection. The diagnostic clue is focal increased ^{18}F-FDG uptake along the lead (Figure 2). Focal increased uptake in a patient with concern for lead infection should prompt complete removal of the device and leads. ^{18}F-FDG PET/CT may not be able to easily detect an intra-cardiac vegetation at the tip of the lead given the small size and also moving vegetation in a background of physiologic cardiac ^{18}F-FDG activity. On the other hand, vegetation detected on PET indicates an ongoing infection and guarantees entire device removal. Although TTE and TEE can also identify intra-cardiac lead vegetation, they can be chronic or treated—not representative of active infection.[7]

Infection can present in any of these regions of a CIED with the qualitative appearance of focal increased uptake. Inflammatory change potentially may be differentiated from infection based on a more homogeneous pattern of relatively less increased ^{18}F-FDG uptake (Figure 3). Increased signal on ^{18}F-FDG PET due to inflammation resolves within 4-8 weeks after implantation of the CIED.[6] Negative cases generally show no ^{18}F-FDG activity along the devices (Figure 4).

Clinical pitfalls and mimics

Common causes of false negatives are previously treated infections, or sometimes less severe infections.

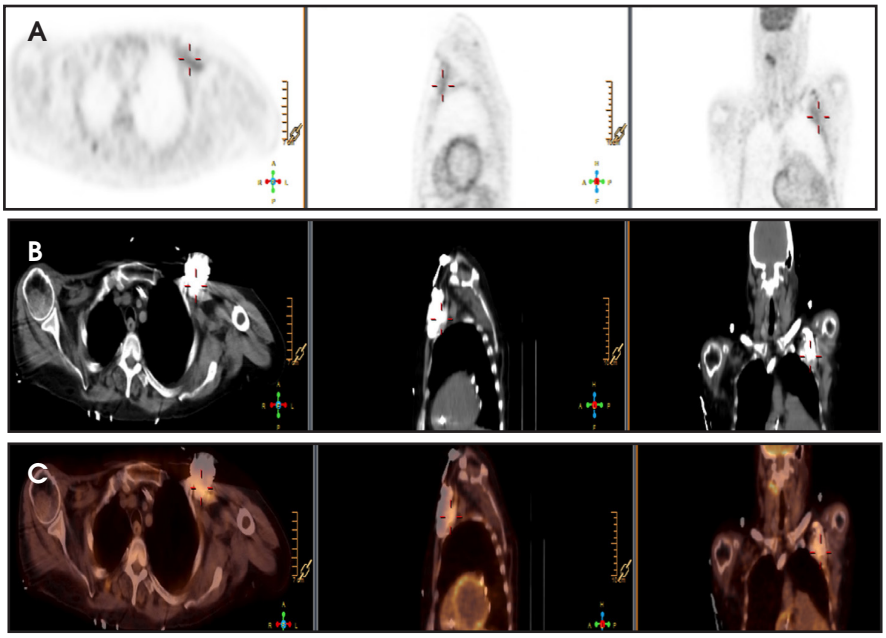

FIGURE 3. *An example of inflammation. The series above demonstrates homogeneous mild linear uptake on ^{18}F-FDG PET along the posterior portion of the pocket in the left upper chest wall, representing post-surgical inflammatory change. Axial (left), sagittal (middle) and coronal (right) views of PET alone (A), CT (B) and fused PET/CT (C) images.*

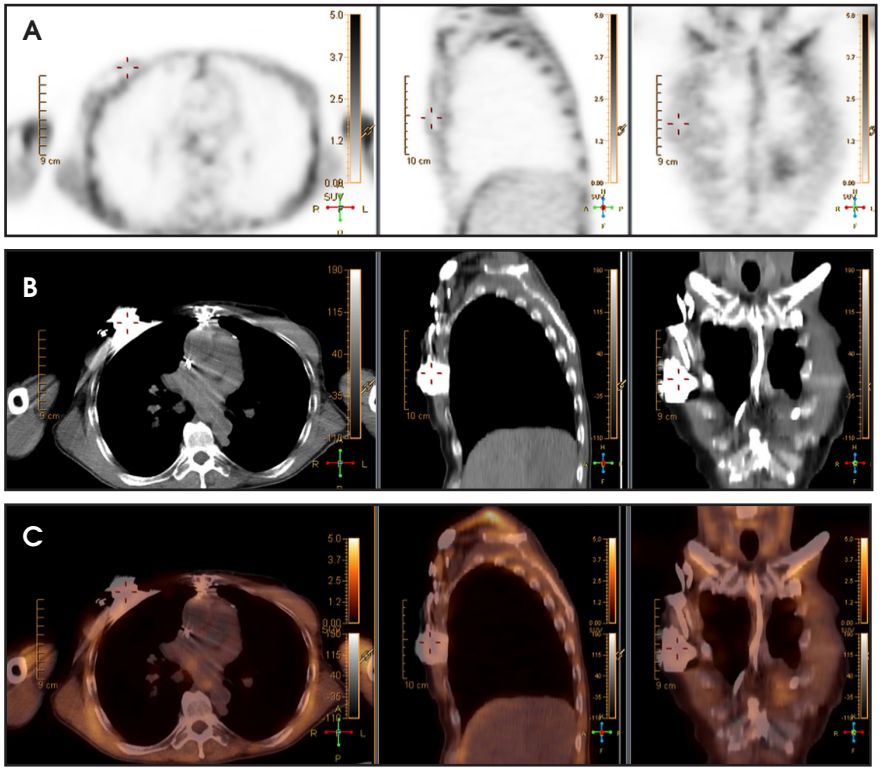

FIGURE 4. *An example of negative CIED infection. No significant focal increased ^{18}F-FDG uptake is seen on PET in the region of the CIED in the right upper chest wall. A negative study suggests that no device removal is necessary, even if there is strong clinical concern for CIED infection. In these cases, patients have been found to respond to IV antibiotics alone with a negative 18F-FDG PET/CT. Axial (left), sagittal (middle) and coronal (right) views of PET alone (A), CT (B) and fused PET/CT (C) images.*

There are reported cases of patients with suspicion for CIED infection and without increased ^{18}F-FDG uptake on PET.[8] Nevertheless, in negative studies patients demonstrated good outcomes with a course of intravenous antibiotics alone and did not require device removal. These results suggest that ^{18}F-FDG PET/CT could have a greater role than diagnosis alone by also helping to guide management decisions. Hyperglycemia is another important cause of false negatives.[8]

Since ^{18}F-FDG PET/CT is primarily utilized to exclude infection or to understand the extent of a suspected infection, in most cases the pre-test probability for infection is high. Therefore, false positives may be less of a concern clinically. Without ^{18}F-FDG PET/CT evaluation, clinicians would often have little option except to remove the CIED in a suspected infection.

False positives can be caused by artefactual uptake due to metallic objects when CT attenuation correction is used to post-process the PET data. For this reason, it is suggested that non-attenuation corrected images be evaluated for cases of potential CIED infection in ^{18}F-FDG PET/CT (Figure 5). A Dacron pouch can also cause a false positive.[8] Thrombus, which can commonly be seen along lead tracts can also demonstrate increased ^{18}F-FDG uptake on PET and cause a false positive.[9]

Conclusion

The qualitative appearance of focal increased uptake is the most reliable way to distinguish infection from inflammation. The latter generally appears homogeneous with low intensity within 4-8 weeks in the case of a recently implanted device.

If there is increased uptake on ^{18}F-FDG PET/CT only in the superficial tissues or if the patient is infected clinically, yet demonstrates no increased uptake in the region of the CIED on ^{18}F-FDG PET/CT, then the infection can be treated with IV antibiotics without removal of the device. If there is increased uptake within the pocket of the

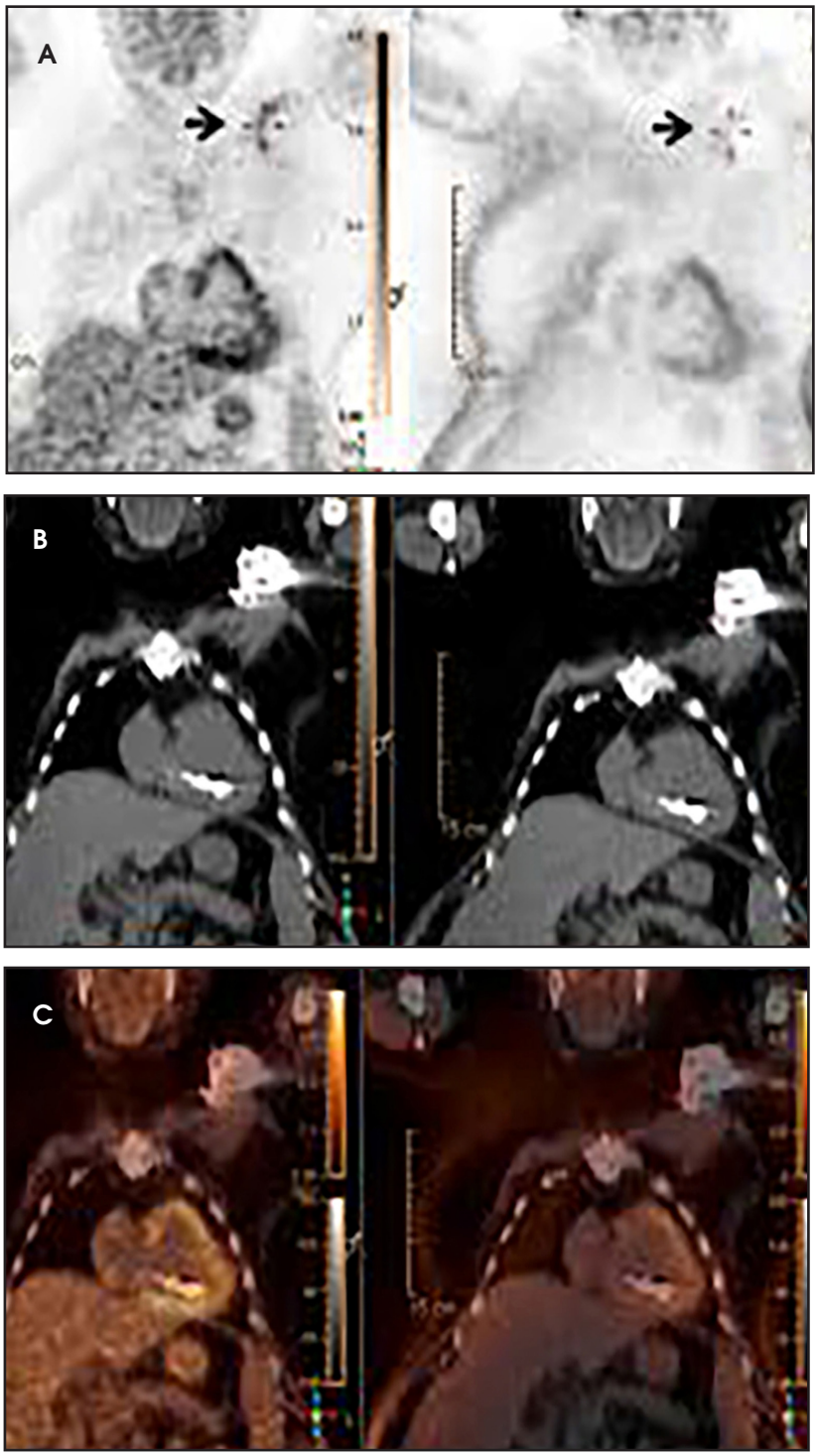

FIGURE 5. *Attenuation-correction artifact. In evaluating a CIED device infection on PET, it is important to not rely on attenuation-corrected images alone, but to compare to the non-attenuation correction series. High attenuation of metallic objects can cause artefactual appearance of increased uptake on attenuation-corrected ^{18}F-FDG PET images. On the left is an attenuation-corrected image which, if reported as increased uptake, would be a false positive. On the right is a non-attenuation-corrected image, which shows no evidence of increased uptake, confirming this finding is artefactual. (A) PET alone, (B) CT, and (C) fused PET/CT images.*

CIED, particularly focal uptake near the device itself or deep to the device, then infection is likely and the device and leads should be removed. Finally, focal increased uptake along a lead wire, but not diffuse mild uptake, is also concerning for lead infection.

Avoid using attenuation-corrected images alone to interpret PET uptake in the setting of CIED infection as this can lead to false positives. Although false negatives occur, they may occur in the setting of less severe infection or treated infection. When infection is suspected clinically, a negative ^{18}F-FDG PET/CT study correlates with clinical response to IV antibiotic treatment alone.

The potential ability to spare some patients the risks (improving quality) and decrease the healthcare system cost of unnecessary CIED removal and replacement supports the use of ^{18}F-FDG PET/CT for evaluation of suspected CIED infection in the era of value-based care.

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