FDG-PET in Large Vessel Vasculitis

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1. Introduction

[¹⁸F]FDG-PET, a non-invasive metabolic imaging technique, is based on the regional distribution of fluorine-18-fluorodeoxyglucose ([¹⁸F]FDG) reflecting increased glucose consumption of tissues. This technique has become increasingly important over the years in the management of patients with malignancies, as many malignant tumors show an enhanced glucose metabolism¹. [¹⁸F]FDG uptake in infections and other inflammatory changes seen during oncologic imaging showed indications for the versatility of [¹⁸F]FDG-PET. Activated leukocytes also overexpress glucose transporters and avidly accumulate glucose and [¹⁸F]FDG ²,³, providing an important rationale for its use in vasculitis. Remarkable images of patients with active vasculitis have been generated through [¹⁸F]FDG-PET scans⁴-¹². Such images demonstrate the potential of [¹⁸F]FDG-PET for a variety of applications which implies that it may also be useful in the future for the routine evaluation of patients with several forms of vasculitis, particularly for large vessel vasculitis.

The family of vasculitides is categorized with reference to the size of vessels involved into large, medium, and small vessel vasculitis (Table 1). Of interest with respect to [¹⁸F]FDG-PET imaging is the group of large vessel vasculitides (giant cell arteritis and Takayasu’s arteritis), other causes of aortitis and potentially also chronic periaortitis. Patients of both of these diseases regularly present a set of non-specific symptoms and laboratory tests which make their diagnosis and follow-up quite challenging. Consequently, patients may receive delays or even unsuccessful diagnostic work-up regarding their condition. The use of whole-body scanning via [¹⁸F]FDG-PET may provide a sensitive metabolic imaging modality that could lead to a more successful and shorter diagnostic workup.

The total amount of available data on [¹⁸F]FDG-PET in large vessel vasculitis is however still limited (Table 2). In addition, no standardized guidelines are in place for the placement of [¹⁸F]FDG-PET imaging in the sequence of the diagnostic workup, its performance, interpretation and description. This chapter summarizes current clinical data in order to assist nuclear medicine and rheumatology practitioners in recommending, performing and interpreting the results of [¹⁸F]FDG-PET in patients with suspected large vessel vasculitis.

2. Giant cell arteritis

Giant cell arteritis was first described by Hutchinson in 1890 as a granulomatous vasculitis of large and medium sized arteries ¹³. Giant cell arteritis usually affects the cranial branches...
of the arteries originating from the aortic arch, particularly the superficial temporal artery; however, involvement of the entire aorta and of its main branches also occurs in about 15% 14. Giant cell arteritis is common in the Caucasian population, with an incidence of about 18 per 100,000 over 50 years of age 15-17 and affects women twice as often as men 15-17. Autopsy studies however suggest that it may be much more common than is clinically apparent 18.

<table>
<thead>
<tr>
<th>Size of vessels</th>
<th>Type of vasculitis</th>
<th>Classification Criteria*</th>
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<tbody>
<tr>
<td></td>
<td>Giant cell arteritis</td>
<td>Age at onset of disease ≥50 yr</td>
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<td></td>
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<td>New headache</td>
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<td>Temporal artery abnormality</td>
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<td>Elevated erythrocyte sedimentation rate</td>
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<td>Abnormal findings on biopsy of temporal artery</td>
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<tr>
<td>Large</td>
<td>Takayasu’s arteritis</td>
<td>Age at onset of disease ≤40 yr</td>
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<td></td>
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<td>Claudication of an extremity</td>
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<td></td>
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<td>Decreased brachial artery pulse</td>
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<td>Difference in systolic blood pressure between arms</td>
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<td>A bruit over the subclavian arteries or the aorta</td>
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<td>Narrowing or occlusion of the entire aorta at angiography</td>
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<td>Medium</td>
<td>Peri-arteritis nodosa</td>
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<td>Essential cryoglobulinaemic vasculitis</td>
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<td>Cutaneous leukocytoclastic angiitis</td>
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*Diagnosis of giant cell arteritis: at least 3/5 criteria; Sensitivity =93.5%, Specificity =90.5%
*Diagnosis of Takayasu’s arteritis: at least 3/6 criteria; Sensitivity =91.2%, Specificity =97.8%

Table 1. Classification of vasculitis

Currently, the etiology of giant cell arteritis still remains unknown. Classic histological pictures of giant cell arteritis show granulomatous inflammation wherein giant cells are usually located at the connection between the intima and media. However, panarteritides with mixed-cell inflammatory infiltrates of lymphomononuclear cells, occasional neutrophils and eosinophils, but without giant cells are also found 19. The focal arteritic lesions cause ischemia which subsequently leads to the sudden or gradual onset of symptoms and a variety of systemic manifestations. A variety of systemic symptoms may be present 20,21, and include myalgia, neck pain, scalp tenderness, jaw claudication, fever,
tenderness of the temporal arteries, transient ischemic attacks, general malaise, fatigue, anorexia, weight loss, depression, and night sweats. Headache is probably the most frequent symptom which occurs in two thirds of patients. Headache is probably the most frequent symptom which occurs in two thirds of patients.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Takayasu arteritis (number of patients)</th>
<th>Giant cell arteritis (number of patients)</th>
<th>Follow-up PETs</th>
<th>Reference</th>
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<tr>
<td>Blockmans et al.</td>
<td>1999</td>
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*Giant cell arteritis and polymyalgia rheumatica patients

Table 2. Clinical studies on PET in the detection of large vessel inflammation: the present literature

3. Takayasu's arteritis

Takayasu's arteritis is named after Mikito Takayasu, who in 1908 had reported the peculiar wreath-like arteriovenous anastomoses around the papillae in a young woman with pulseless disease. This large vessel vasculitis primarily affects the aorta, its main branches, and the coronary and pulmonary arteries. The incidence rate of the disease is about 2 per 1,000,000 with its onset at a mean of 35 years of age. Takayasu's arteritis occurs worldwide, although it is considered to be more common in the Orient and is 10 times more prevalent in females than in males. The etiology of Takayasu's arteritis also remains unresolved, while the clinical course includes both an early and a late phase. Pathology studies in the early phase reveal granulomatous or diffuse productive
inflammation in the media and adventitia, with secondary thickening of the intima and occasional perivascular inflammation. In the clinic, it is commonly the setting of fever of unknown origin with non-specific systemic symptoms. Contrary to the early phase, pathology studies in the late phase show marked thinning of the media, with disruption of elastic fibers, fibrotic thickening of the adventitia, and marked intimal proliferation. The resulting variable ischemic symptoms secondary to arterial stenosis, occlusion, or arterial dilatation and aneurysmal formation cause various clinical conditions, such as arm claudication, decreased arterial pulses, carotodynia, visual loss, stroke, aortic regurgitation and arterial hypertension. Topological classification of Takayasu’s arteritis is based on the vascular provinces that are affected, with either affection of the branches of the aortic arch (Type I), the ascending aorta, aortic arch and its branches (Type IIa), the ascending aorta, aortic arch and its branches and the thoracic descending aorta (Type IIb), the thoracic descending aorta, abdominal aorta, and/or renal arteries (Type III), the abdominal aorta and/or renal arteries (Type IV) or combined features of types IIb and IV.

### 4. Diagnostic work-up in large vessel vasculitis

Giant cell arteritis and Takayasu’s arteritis are both usually present with a wide clinical spectrum with no specific laboratory finding. The American College of Rheumatology has established a set of clinical, radiological and histological criteria to classify cases of biopsy-proven arteritis. The presence of at least three of the described criteria is required for classifying a patient as having either Takayasu’s arteritis or giant cell arteritis. These criteria provide a sensitivity of 93.5% with a specificity of 90.5% for diagnosing giant cell arteritis and a sensitivity of 91.2% with a specificity of 97.8% for diagnosing Takayasu’s arteritis in biopsy-positive patients. Although these criteria were originally designed for research purposes to help distinguish between different types of vasculitis; they are in clinical practice also frequently used for diagnosing an individual patient. Nevertheless, the fact that frequent symptoms of giant cell arteritis such as jaw claudication, diplopia, neck pain, and elevated C-reactive protein are not included in the criteria, limits their widespread clinical application. Criteria that are included, such as headache and scalp tenderness can also be due to various other diseases. A normal erythrocyte sedimentation rate does not rule out giant cell arteritis, as it has been found in up to 30% of patients with biopsy-proven giant cell arteritis. Furthermore, several patients with giant cell arteritis do only display nonspecific symptoms that does not apply to any set of criteria. Systemic giant cell arteritis symptoms such as fever, anorexia, weight loss and malaise may focus the diagnostic work-up towards a suspected malignancy, especially in older patients.

Frequent clinical features of Takayasu’s arteritis such as fever, postural dizziness, arthralgias, weight loss, headache, hypertension, elevated erythrocytes sedimentation rate and anemia were also not included in the classification criteria of the American College of Rheumatology. In contrast, angiographic findings and non-congruent blood pressure measurements between both arms are included as part of the diagnostic criteria although they may be false negative in early vasculitis, or when the arteritis is restricted to the abdominal aorta, its branches, or to the pulmonary artery.

The wide clinical spectrum and the diagnostic limitations of giant cell arteritis and Takayasu’s arteritis frequently cause delay in their diagnosis and subsequent treatment.
5. \[^{18}\text{F}]\text{FDG-PET and }[^{18}\text{F}]\text{FDG-PET/CT}

\[^{18}\text{F}]\text{FDG-PET is an operator-independent, non-invasive imaging modality which examines the regional distribution of fluorine-18-fluorodeoxyglucose. Deoxyglucose is labeled with the positron emitting radionuclide, }^{18}\text{Fluorine, and is intravenously administered to patients. }[^{18}\text{F}]\text{FDG initially distributes in proportion to the perfusion of the organs, where it follows the same route of uptake as glucose. After entering cells through specific carriers, }[^{18}\text{F}]\text{FDG is phosphorylated to }[^{18}\text{F}]\text{FDG-6-phosphate, trapped intracellularly, but not metabolized further. The emitted positrons can be detected by a scanner and are displayed as a bright signal in the }[^{18}\text{F}]\text{FDG-PET scan, reflecting an increased glucose requirement.}

Heightened glucose metabolism is a property of many malignancies, a fact which has fostered the use of \[^{18}\text{F}]\text{FDG-PET studies in the staging and follow-up in various types of cancers}^{1}.

Modern PET-CT scanners combine PET scanners with a computed tomography scanner in a single gantry system. With these scanners, images are taken sequentially with both devices in the same session and the reading can be done with the single co-registered image. As a consequence, the functional image obtained by PET, can be correlated more precisely with the anatomic structures. PET/CT has shown an incremental diagnostic value over CT and PET alone and there is emerging evidence of a substantial impact of PET/CT imaging on patient management^{40}.

6. \[^{18}\text{F}]\text{FDG-PET scanning protocols for large vessel vasculitis}

The American and the European Association of Nuclear Medicine have both established procedure guidelines for tumor imaging with \[^{18}\text{F}]\text{FDG-PET}^{41,42}. The guidelines of the American Association of Nuclear Medicine from 1998 recommend fasting at least 4 hours prior to the scan. Low blood glucose levels are recommended, the injected activity should total 350 to 750 MBq \[^{18}\text{F}]\text{FDG, and image acquisition should start 30 to 40 minutes after injection. In contrast, the guidelines of the European Association of Nuclear Medicine from the year 2003 advocate fasting at least 6 hours prior to the scan. Blood glucose level should not exceed 130mg/dl, the injected \[^{18}\text{F}]\text{FDG activity should be 6 MBq/kg body weight, and acquisition should be started 60 minutes after injection.}

Both professional associations however, have not established guidelines for the PET imaging of inflammation and consequently, the present studies (Table 2) have used several different protocols. Pre-scan fasting intervals of 4 hours^{43,44}, 6 hours^{45-47}, and overnight fasts^{48-50} were applied. Body-weight adapted protocols for the applied \[^{18}\text{F}]\text{FDG dose with 5}^{49}, 6^{50} or 6.5 MBq^{46,51} \[^{18}\text{F}]\text{FDG per kilogram bodyweight were used. However, fixed doses of 296 MBq}^{52}, 370 MBq^{48}, and 450 MBq^{47} were also employed. To accelerate renal \[^{18}\text{F}]\text{FDG elimination, one group also routinely administered additional furosemide}^{45}. Most studies on \[^{18}\text{F}]\text{FDG-PET in large vessel vasculitis did not restrict scanning by maximal glucose levels and only three studies tolerated maximum serum glucose levels of 100mg/dl}^{48,52} and 180mg/dl^{49}. Large differences in the time interval between \[^{18}\text{F}]\text{FDG application and image acquisition were also shown as }[^{18}\text{F}]\text{FDG-uptake periods of 45 minutes}^{49,50}, 60 minutes^{45,46,48,51,52}, or 90 minutes^{43,44,47} were reported. Dedicated PET scanners with full-ring detectors were generally used; nevertheless, hybrid cameras have also been successfully employed^{48,52,53}. Reports on the use of combined \[^{18}\text{F}]\text{FDG-PET-CT scanners in large vessel vasculitis are available}^{50,54,55}.
The average radiation dose from the $^{18}$F-FDG-PET scan is 7mSv, the average dose from the CT scan is 18mSv. The CT dose, however, can be lowered by the use of low-dose acquisition protocols.

This summary indicates that despite a lack of standardization, $^{18}$F-FDG-PET is a reliable imaging modality of large vessel vasculitis.

### 7. $^{18}$F-FDG-PET and Atherosclerosis

The accumulation of glucose analogues has not only been demonstrated in vasculitic vessels, but also in atherosclerotic plaques (Figure 1)\(^{56}\). Consequently, a modest large vessel $^{18}$F-FDG accumulation at the level of the major vessels occurs in about 50% of all PET-scans, with increased prevalence in older people\(^ {57}\). This vascular uptake might be explained by smooth muscle metabolism in the media, subendothelial smooth muscle proliferation from senescence, and the presence of macrophages within the atherosclerotic plaque. Therefore, vascular uptake found in the $^{18}$F-FDG-PET scan is not specific for vasculitis.

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**Fig. 1.** 71-year-old female patient that underwent FDG-PET/CT to evaluate a suspicious lung nodule. Focal FDG uptake was found in the thoracic and abdominal aorta corresponding to circumscribed atherosclerotic and aneurysmatic wall changes (arrow; from the Institute of Nuclear Medicine, University Hospital, Bern, CH)
Nevertheless, atherosclerotic lesions can be differentiated from vasculitic lesions by taking into account the vascular distribution, $[^{18}F]$FDG uptake pattern, and the intensity of the $[^{18}F]$FDG accumulation. For example, the internal carotid artery demonstrates atherosclerotic changes more frequently, while the external carotid artery more often reveals inflammatory changes. The uptake pattern of atherosclerotic mediastinal great vessels sometimes can be identified as ring-shaped structures, while contrary to this, the uptake pattern in the arteries of the abdomen and lower extremities are often linear and continuous. Most discriminatively, atherosclerotic lesions rarely demonstrate intense uptake of FDG.

To distinguish vasculitis from atherosclerosis, a visual scoring of vascular $[^{18}F]$FDG-uptake compared to the liver $[^{18}F]$FDG-accumulation has been established. Three grades of large vessel $[^{18}F]$FDG-uptake are differentiated (Figure 2): a) Grade I: uptake present but lower than liver uptake, b) Grade II: similar to liver uptake, and c) Grade III: uptake higher than liver uptake. Proposed by Meller et al., this scale was subsequently validated to represent the severity of inflammation.

So far, this score has been employed in two reference collectives without clinical symptoms or laboratory signs of large vessel inflammation in order to determine the uptake in non-vasculitic vessels. Grade I vessel uptake was frequently found in the thoracic part of the aorta which was most likely due to atherosclerosis. Accordingly, only Grade II or III $[^{18}F]$FDG-uptake in the thoracic aorta and any visible uptake in other segments should routinely be judged as active large vessel inflammation. In this manner, the majority of lesions can be ruled out as due to atherosclerosis. On the other hand, computed quantification of $[^{18}F]$FDG-uptake using the $[^{18}F]$FDG standardized uptake value (SUV) has not shown to be useful in discriminating atherosclerosis from vasculitis yet.

### 8. $[^{18}F]$FDG-PET for diagnosing giant cell arteritis

The diagnosis of giant cell arteritis is currently based mainly on clinical evaluation, laboratory results, and temporal biopsy, but a gold standard is lacking. Despite recent advances, no imaging modality has been included in the American College of Rheumatology diagnostic criteria for giant cell arteritis (Table 1). Nevertheless, $[^{18}F]$FDG-
PET has indicated its usefulness clinically for a number of studies through better evidence, as compared to Takayasu’s arteritis, due to the higher frequency of the disease (Table 2). The uptake pattern in large vessels affected by giant cell arteritis was linear, continuous, and was predominantly of Grade II. The thoracic vessels were most frequently affected, followed by the abdominal vessels. In the published studies, the ability of $^{18}$F-FDG-PET to detect large vessel inflammation differed considerably. In studies employing patients with polymyalgia rheumatica and giant cell arteritis, sensitivities between 56% and 100% were reported, with a specificity between 77% and 98%. The large differences seen between the studies can partially be explained by dissimilar disease activity; as suggested by one study demonstrating that the sensitivity depends on the degree of inflammation (Figure 4). C-reactive protein has shown to be a better predictor for the sensitivity of $^{18}$F-FDG-PET in giant cell arteritis than the erythrocyte sedimentation rate.

Studies employing $^{18}$F-FDG-PET and Magnetic Resonance Imaging (MRI) revealed comparable sensitivities for both methods. $^{18}$F-FDG-PET may have the advantage that it simultaneously identifies more affected vessels, possibly reflecting the fact that metabolic changes normally precede morphologic changes in giant cell arteritis. Additionally, $^{18}$F-FDG-PET might also allow new insights into the pathology of giant cell arteritis and polymyalgia rheumatica. A study demonstrated inflammation of the aorta or its major branches in 92% of patients with polymyalgia rheumatica. Tracer uptake was strongly correlated with the erythrocyte sedimentation rate and the C-reactive protein. These data underline that polymyalgia rheumatica frequently may be accompanied by subclinical vasculitis.

$^{18}$F-FDG-PET also offers the possibility of whole-body screening in one procedure which may become helpful in the follow-up of patients with giant cell arteritis. The results of computed quantification of vascular $^{18}$F-FDG accumulation correlate well and better than Magnetic Resonance Imaging with the clinical course also at longitudinal follow up.

The value of $^{18}$F-FDG-PET for diagnosing temporal arteritis has however been questioned in a study of 22 patients, 17 of which had involvement of the temporal arteries which was not detected by $^{18}$F-FDG-PET. The high $^{18}$F-FDG uptake of the brain and the small diameter of the temporal arteries limited its sensitivity in the detection of cranial vessel involvement with the whole-body PET technique used. Newer generation PET/CT scanners offer an image resolution corresponding to a three-fold improvement compared to the technology used in the aforementioned study (2mm vs. 7mm), potentially allowing to image even smaller arteries as the temporal arteries. Further clinical studies must are warranted to clarify the potential role of PET in the non-invasive work-up of temporal vasculitis.

9. $^{18}$F-FDG-PET for diagnosing Takayasu’s arteritis

The diagnosis of Takayasu’s arteritis frequently integrates imaging and angiographic (Table 1). However, angiographic alterations usually occur in the late phase of Takayasu’s arteritis while metabolic changes are already present in the early phases. The data on the use of $^{18}$F-FDG-PET in Takayasu’s arteritis are less robust compared to those in giant cell arteritis (Table 2), accounting for the different prevalences of both vasculitides. During the early phase of Takayasu’s arteritis, the $^{18}$F-FDG uptake pattern is linear and continuous (Figure 3A), while in the late phase the pattern can become patchier rather than continuous but still remains in a linear distribution. Three studies reported sensitivities of $^{18}$F-FDG-PET between 83% and 100%. This is comparable to Magnetic Resonance Imaging...
FDG-PET in Large Vessel Vasculitis

Imaging. Additionally, metabolic imaging using $[^{18}F]FDG$-PET for Takayasu’s arteritis has identified more affected vascular regions than morphologic imaging using Magnetic Resonance Imaging. However, unlike Magnetic Resonance Imaging, $[^{18}F]FDG$-PET does not give any information about the wall structure or the lumen of affected vessels. Similarly to giant cell arteritis, there is a clear correlation between the activity of vessel inflammation and the sensitivity of $[^{18}F]FDG$-PET. $[^{18}F]FDG$-PET positive patients have shown significantly higher erythrocyte sedimentation rates and C-reactive protein levels as compared to $[^{18}F]FDG$-PET negative patients, with the C-reactive protein being the superior marker.

Follow-ups in Takayasu’s arteritis only based on clinical symptoms alone have shown to be of limited accuracy. In a previous report, biopsies showed active inflammation in 44% of patients thought to be in clinical remission. However, $[^{18}F]FDG$-PET is able to detect more sites than just those that were clinically active. This makes $[^{18}F]FDG$-PET a promising candidate to be regularly employed in the follow-up of Takayasu’s arteritis (Figure 3) due its high sensitivity and the good correlation with the outcome.

Fig. 3. A) $[^{18}F]FDG$-PET of a patient with Takayasu’s arteritis with markedly abnormal uptake of $[^{18}F]FDG$ in the aortic arch and carotid arteries (arrows). B) $[^{18}F]FDG$-PET scan of the same patient in clinical remission after treatment with prednisone and intravenous cyclophosphamide (from reference 43)

10. $[^{18}F]FDG$-PET-CT in large vessel vasculitis

The combination of $[^{18}F]FDG$-PET scanners with Computed Tomography (CT) has gained importance in the management of patients with malignancies by allowing the integration of morphologic and metabolic information for detection, staging, and therapy control. Rapidly increasing availability of $[^{18}F]FDG$-PET-CT scanners are also opening new opportunities for its application in rheumatology by allowing the investigation of both morphologic and metabolic activity while significantly improving the localization of affected vessels. Two case reports have already indicated the value of $[^{18}F]FDG$-PET-CT.
Fig. 4. Sensitivity of Large Vessel Vasculitis $[^{18}F]$FDG-PET as a function of C-reactive protein (CRP) levels and erythrocyte sedimentation rate (ESR), respectively. High sensitivity for detection of large vessel vasculitis is reached at high CRP and ESR levels (from reference 49).

Fig. 5. 52 year-old female patient with clinical suspicion of a large vessel vasculitis. The FDG-PET/CT shows intense tracer uptake along the aortic arch, the supraaortic branches and the supraclavicular arteries. There is also uptake along the abdominal aorta and femoral arteries and branches.
Fig. 6. FDG-PET/CT of a 67-year-old male patient with recent loss of weight and continuous deterioration of his general condition. The PET/CT performed did not support the clinical suspicion of a malignant tumor but showed intense vessel uptake (A). Additional high-resolution PET images of the chest and neck illustrate the ability of state-of-the-art PET machines to visualize circumscribed wall inflammation even in medium sized arteries as the carotic sinus and the vessel wall of the aortic arch (B).

Scanners in large vessel vasculitis \(^{53,54}\) and one clinical trial has investigated its value in 14 patients \(^{50}\). The co-registered CT scan was most useful for the anatomic identification of vascular \(^{18}\)F-FDG-uptake, especially in case of rather moderate \(^{18}\)F-FDG-accumulation. Furthermore, the anatomic identification of mediastinal \(^{18}\)F-FDG uptake, particularly in the pulmonary arteries was significantly improved (Figure 5). The coregistered CT scan allows for a sensitive detection of calcified plaques to discriminate vasculitis from inflammatory arteriosclerotic changes.

11. Conclusions

In conclusion, whole-body imaging with \(^{18}\)F-FDG-PET is highly effective in assessing the extent of giant cell arteritis and Takayasu’s arteritis, respectively. \(^{18}\)F-FDG-PET has shown to have identified more affected vascular regions than morphologic imaging with Magnetic Resonance Imaging in both diseases. A unique feature and strength of FDG-PET is the opportunity to monitor disease activity non-invasively. In contrast to other imaging modalities PET allows for an immediate assessment of response to anti-inflammatory treatment and is suitable to guide therapy. Recent developments in PET technology such as integrated PET/CT machines and increased image resolution of the PET submodality imply significant improvements for vasculitis imaging with FDG. Further studies are warranted to evaluate the diagnostic benefit of these newer technical developments.
[18F]FDG-PET has the clear potential to develop into a valuable tool in the diagnostic work-up of both giant cell arteritis and Takayasu's arteritis, and may become a first-line investigation technique for non-invasive therapy monitoring. However, consensus regarding the imaging procedures as well as further clinical evidence is urgently needed.

12. References


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This book represents the culmination of the efforts of a group of outstanding experts in vasculitis from all over the world, who have endeavored to draw themselves into this volume by keeping both the text and the accompanying figures and tables lucid and memorable. The book provides practical information about the screening approach to vasculitis by laboratory analysis, histopathology and advanced image techniques, current standard treatment along with new and more specific interventions including biologic agents, reparative surgery and experimental therapies, as well as miscellaneous issues such as the extra temporal manifestations of "temporal arteritis" or the diffuse alveolar hemorrhage syndrome. The editor and each of the authors invite you to share this journey by one of the most exciting fields of the medicine, the world of Vasculitis.

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