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## **PET/CMR: one more step toward non-invasive morpho-functional diagnosis of cardiac malignancies**

**Brief Title:** PET/MRI of cardiac malignancies

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Cardiac malignancies are rare, including primary and metastatic neoplasms developing either by systemic spread or tumor direct extension. In patients with cardiac masses, it is mandatory to accurately define their malignant potential, the exact anatomic location, and the response to treatment in order to optimize therapeutic strategy. In the last years, cardiac magnetic resonance imaging (CMR) and multi-tracers positron emission tomography/computed tomography (PET/CT) have revolutionized the non-invasive diagnosis of cardiac tumors, allowing precise morphological and functional disease characterization. Nowadays, co-registered imaging from PET/MR devices or combined from separately acquired CMR and PET images, represents a great technological development able to influence clinical decisions. Herein, we didactically present PET, CMR, and fused PET/CMR images highlighting the strengths of such combined morpho-functional investigation in five selected patients with cardiac malignancies and addressed for tumor aggressiveness evaluation, lesion topographic assessment, disease extension definition, or treatment efficacy evaluation.

**FIGURE 1. Evaluation of mass aggressiveness: right ventricle cardiac metastasis.**

A 83-years-old man with previous history of clear cell renal cell carcinoma (CCRCC) presented with chest pain and acute heart failure. Trans-thoracic echocardiography revealed a right ventricle mass. Cardiac magnetic resonance imaging (CMR) demonstrated a voluminous intracavitary tissular mass (arrows) originating from right ventricle wall and infiltrating the pericardium. Lesion showed intermediate signal intensity on dark-blood images (A), diffuse hyperintensity on T2-weighted fat-saturated dark-blood images (B), and heterogeneous enhancement on delayed post-contrast inversion recovery sequences (C). Positron emission tomography (PET) (D), and PET and CMR hybrid images (arrow) (E) revealed intense <sup>18</sup>F-fluorodeoxyglucose (<sup>18</sup>F-FDG) uptake on cardiac lesion (SUVmax: 14.1), suggesting a malignant origin. Pathologic diagnosis of CCRCC (F) was reached after pericardial biopsy (HE x 200, cytokeratin (AE1/AE3) positive x 400). This case highlights the central role of PET/CMR in the non-invasive diagnosis of cardiac malignancies.

**FIGURE 2. Definition of cardiac tumoral extension: locally infiltrating right ventricle metastasis from vulvar carcinoma.**

A 82-years-old woman with history of vulvar carcinoma underwent follow-up <sup>18</sup>F-fluorodeoxyglucose positron emission tomography/computed tomography (<sup>18</sup>F-FDG PET/CT). Large area of intense and heterogeneous glucose metabolism (SUVmax: 10.2) involving the right ventricle wall was revealed on PET/CT (A,B) images (arrow). A metastatic cardiac involvement was suggested. Cardiac magnetic resonance imaging (CMR) confirmed tumoral right ventricle involvement with pericardial invasion. A 38 x 24 mm infiltrating mass of right ventricle wall with mobile intracavitary component and intermediate signal intensity was distinguished on dark-blood images (C). Cardiac lesion was characterized by heterogeneous hyperintensity on T2-weighted fat-saturated dark-blood images (D), and heterogeneous contrast enhancement with central hypointense area (E). Tumor heterogeneity was clearly showed on PET and CMR hybrid images (F). This case highlights the interest of PET/CMR for the assessment of cardiac tumor local extension.

**FIGURE 3. Multi-parameter tissular characterization: right atrial metastasis from cutaneous melanoma**

A 69-years-old man with stage-IV melanoma treated by surgery, chemotherapy, and immunotherapy presenting with a right atrium asymptomatic mass revealed on echocardiography. Cardiac magnetic resonance imaging (CMR) confirmed the presence of atrial lesion (arrows) with intermediate signal intensity on T1-weighted dark-blood (A), T2-weighted fat-saturated dark-blood images (B), and steady-state free precession sequences (C). Minimal pericardial effusion was also showed. T1- and T2-mapping images revealed a short T1 (600 ms vs. 1030 ms in normal myocardium) (D), and moderately increased T2 (60 ms vs. 50 ms in normal myocardium) (E). Atrial lesion presented moderate and heterogeneous gadolinium enhancement (F) and intense fluorodeoxyglucose (<sup>18</sup>F-FDG) uptake (SUV: 9.3) on positron emission tomography/computed tomography (PET/CT) (G), and PET and CMR hybrid images (H). This case highlights the potential interest of combined morpho-functional quantitative parameters as native T1- and T2-mapping values and SUVmax for tumors characterization, particularly useful for melanoma metastases.

**FIGURE 4. Tissular characterization by specific radiotracers: left atrial appendage metastasis from neuroendocrine tumor.**

A 52-years-old women addressed for primary staging of metastatic neuroendocrine tumor (NET) of unknown origin. Transthoracic echocardiography was normal. Intense focal uptake (SUVmax: 7.3) of 6-L-<sup>18</sup>F-fluorodihydroxyphenylalanine (<sup>18</sup>F-FDOPA) was showed on

positron emission tomography/computed tomography (PET/CT) in the upper wall of left atrial appendage (**A,D,G**), without abnormalities on coupled CT scan. NET metastasis was suggested (arrows) and patient underwent cardiac magnetic resonance imaging (CMR). A few millimeters nodule imbedded in upper wall of the left atrium was detected on steady-state free precession sequence showing minimal peripheral enhancement on post-contrast acquisition (**B,E,H**). The left atrial nodule was precisely and easily recognized on PET and CMR hybrid images (**C,F,I**). This case suggests that PET/MR with radiotracers specifically targeting neuroendocrine phenotype (i.e.:  $^{18}\text{F}$ -FDOPA,  $^{68}\text{Ga}$ -DOTA-peptides) will increase the non-invasive detection of asymptomatic cardiac metastases in patients with NETs.

**FIGURE 5. Evaluation of treatment efficacy: right atrial involvement of thoracic large B-cell lymphoma.**

A 46-years-old man presented with chest pain and voluminous right upper thoracic mass. Staging echocardiography was normal. Lesion biopsy revealed diffuse large B-cell lymphoma. Pre-treatment positron emission tomography/computed tomography (PET/CT) also showed intense (SUVmax: 12.3), pathologic, and multifocal right atrial  $^{18}\text{F}$ -fluorodeoxyglucose ( $^{18}\text{F}$ -FDG) uptake suggesting cardiac lymphoma extension (**A**). Cardiac magnetic resonance imaging (CMR) confirmed diffuse tissular infiltration of right atrium walls (arrows), minimal pericardial effusion, without adjacent structures invasion on steady-state free precession sequence (**B**). On post-contrast inversion recovery images atrial tumor presented with homogenous hypo-signal compared to normal myocardium (**C**). PET and CMR hybrid images well showed the hypermetabolic atrial tumor infiltration (**D**).  $^{18}\text{F}$ -FDG PET/CT (**E**), CMR (**F-G**), and fused PET and CMR (**H**) early performed after chemotherapy showed complete morpho-functional regression of atrial tumor (dotted arrows). This case highlights the role of PET/CMR in the evaluation of treatment efficacy.











