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Integrated whole-body PET/MR imaging with 18F-FDG, 18F-FDOPA, and 18F-fluorodopamine in paragangliomas, in comparison to PET/CT: NIH first clinical experience with a single-injection, dual-modality imaging protocol

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Abstract

Purpose—Paragangliomas (PGLs) are tumors that can metastasize and recur; therefore, lifelong imaging follow-up is required. Hybrid positron emission tomography (PET)/computed tomography (CT) is an essential tool to image PGLs. Novel hybrid PET/magnetic resonance (MR) scanners are currently being studied in clinical oncology. We studied the feasibility of simultaneous whole-body PET/MR imaging to evaluate patients with PGLs.

Methods—Fifty-three PGLs or PGL-related lesions from eight patients were evaluated. All patients underwent a single-injection, dual-modality imaging protocol consisting of a PET/CT and subsequent PET/MR scan. Four patients were evaluated with 18F-fluorodeoxyglucose (18F-FDG), two with 18F-fluorodihydroxyphenylalanine (18F-FDOPA), and two with 18F-fluorodopamine (18F-FDA). PET/MR data were acquired using a hybrid whole-body 3-Tesla integrated PET/MR scanner. PET and MR data (DIXON images for attenuation correction and T2-weighted sequences for anatomic allocation) were acquired simultaneously. Imaging workflow and imaging times were documented. PET/MR and PET/CT data were visually assessed (blindly) in regards to image quality, lesion detection, and anatomic allocation and delineation of the PET findings.

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Results—With hybrid PET/MR, we obtained high quality images in an acceptable acquisition time (median: 31 min, range: 25–40 min) with good patient compliance. A total of 53 lesions, located in the head-and-neck area (6), mediastinum (2), abdomen and pelvis (13), lungs (2), liver (4), and bone (26) were evaluated. 51 lesions were detected with PET/MR and confirmed by PET/CT. Two bone lesions (L4 body (8 mm) and sacrum (6 mm)) were not detectable on an 18F-FDA scan PET/MR, likely due to washout of the 18F-FDA. Co-registered MR tended to be superior to co-registered CT for head-and-neck, abdomen, pelvis, and liver lesions for anatomic allocation and delineation.

Conclusions—Clinical PGL evaluation with hybrid PET/MR is feasible with high image-quality and can be obtained in a reasonable time. It could be particularly beneficial for the pediatric population and for precise lesion definition in the head-and-neck, abdomen, pelvis, and liver.

Key Terms

pheochromocytoma and paraganglioma; PET/MR; 18F-fluorodeoxyglucose; 18F-fluorodopamine; 18F-fluorodihydroxyphenylalanine

INTRODUCTION

Paragangliomas (PGL) are neuro-endocrine tumors that arise from either chromaffin sympathetic tissues (adrenal and paraganglia of abdomen, pelvis, and posterior mediastinum) or from parasympathetic tissues (head-and-neck and para-cardiac paraganglia). They have a specific cellular metabolism: they are able to synthesize, store, re-uptake, and secrete catecholamines and their metabolites.¹ PGLs can occur either sporadically or in familial syndromes due to germline mutations in susceptibility genes.² When occurring in a familial context, PGLs can occur in young patients.^{3,4} PGLs are slow growing tumors characterized by long term development and can metastasize in the lymph nodes, bones, lungs, and liver. The main treatment for PGL is surgery if the tumors have not metastasized. However, if metastases are present, there are other options: radiation therapy, chemotherapy, targeted therapies, or follow-up without therapy. But unfortunately, there is currently no cure when metastases are present. When a PGL tumor is resected, recurrence is still possible.^{5,6} Thus, lifelong follow-up is required to timely manage a prospective recurrence or tumor growth.^{6,7}

Positron emission tomography (PET) is a comprehensive functional nuclear medicine imaging tool that is used for PGL staging, characterization, and follow-up. Various PET radiotracers are useful in PGLs, including the widely used glucose analog 18F-fluorodeoxyglucose (18F-FDG)⁸ and the newer PGL-specific PET radiotracers, 18F-fluorodopamine (18F-FDA), and 18F-fluorodihydroxyphenylalanine (18F-FDOPA). 18F-FDA is a catecholamine analog and 18F-FDOPA is an amino-acid analog of a catecholamine precursor. Both have shown value in PGL detection and staging.^{9–15} PET has been replaced by hybrid PET/computed tomography (CT) for PGL management (as was done in the whole oncologic field). Indeed, the ability to combine functional information from PET and anatomical information from CT in a single imaging session using hybrid PET/CT has improved the diagnostic performance of PET.¹⁶

Magnetic resonance (MR) imaging also has a long-standing role for imaging PGL. PGLs typically appear highly vascularized and have high signal intensity on T2-weighted images.¹⁷ MR imaging has two advantages over CT when managing PGLs: its very good soft-tissue contrast provides additional information for PGL surgical planning and follow-up, and it does not expose patients to radiation exposure. Thus, it is more appropriate in children and in patients for whom life-long follow-up imaging may be anticipated, where radiation exposure limitation is a major concern.

The development of PET/CT over the last decade has provided great clinical relevance. Hybrid PET/MR has recently become available in clinical oncology and is expected to thrive in this area too. Early reports have described the use of simultaneous whole-body (i.e., from the thighs to the head) PET/MR experience for head-and-neck tumors, neuroendocrine tumors, abdominal tumors, pediatric oncology, lymphomas, and various oncologic diagnoses.^{18–24} Based on these studies, the main expected clinical benefit of PET/MR is the convenience of a “one-stop shop”, shortening the overall acquisition time when both MR and PET are necessary. Additionally, co-registered MR might be of added value compared to co-registered CT when evaluating head-and-neck lesions, tumors of the abdomen and pelvis, and liver lesions (due to better MR soft-tissue contrast). However, in an educational paper written by Martinez-Möller and Eiber and al., following their first experiences with PET/MR, the difficulties linked to the workflow and MR protocols were emphasized.²⁵ Indeed, MR scanning is often complex, time-demanding, and requires more patient cooperation, compared to the fast and easy performance of CT. Excellent interaction of well-trained personnel from different subspecialties is necessary when using PET/MR technology. Adequate workflow protocols must be designed and tested for a variety of clinical indications in order to get the maximum benefit of this new technology.^{25–27} One case report was published using PET/MR imaging in a young patient with a malignant adrenal PGL. In this case report, 124I-MIBG PET/MR allowed a more accurate tumor volume determination, which is of important relevance for pretherapeutic dosimetry.²⁸

The Pheochromocytoma and Paraganglioma Research Program at the National Institutes of Health (NIH) has an extensive long-standing experience with patients suffering from PGLs. Since this program includes an increasing number of pediatric patients and metastatic patients requiring repeated scanning, there is a need for radiation dose limitation and imaging time optimization. Therefore, the aim of this pilot study was to assess the feasibility of whole-body integrated PET/MR for evaluation or reevaluation of patients with PGL. We addressed the applicability in clinical routine (scan duration), the quality of the overall images, and the detectability of PGL lesions with PET/MR compared to PET/CT. With PET-positive lesions, we assessed the feasibility of anatomic allocation and delineation with co-registered anatomic images (i.e., CT or MR imaging) using PET/MR and compared them to PET/CT.

PATIENTS AND METHODS

Setting and patient population

We studied fifty-three PGL lesions in eight patients (two men and six women, with a median age of 49 years (range 34–66)). All patients underwent 18F-FDG, 18F-FDOPA, or 18F-FDA

PET scanning for either their initial evaluation or reevaluation after a previous surgery or for the detection of metastatic disease. All patients were imaged at the NIH. The diagnosis of PGL was based on PGL-specific biochemical findings, imaging results, and clinical follow-up. Among the patients, two patients had one or multiple foci of non-metastatic PGL, and six patients had metastatic PGL. Metastatic PGL was defined by the presence of metastatic lesions at sites where neural-crest-derived tissue is normally absent.²⁹ Patient characteristics are listed in Table 1.

The NIH protocol (00-CH-0093) was approved by the Institutional Review Board of the National Institute of Child Health and Development. All patients provided a signed informed consent. The inclusion criteria were at least one PGL at the time of the study, and the ability to undergo a PET/MR scan after the PET/CT scanning. Exclusion criteria were: pregnancy, age below 18 years, and standard contraindications for MR examinations (unsafe implants, pacemakers, etc.).

Imaging protocol and workflow

All patients underwent a single-injection, dual-imaging protocol that included a PET/CT and a subsequent PET/MR. Consequently, this approach did not require an additional injection of 18F-tracer or any additional radiation exposure to the patients. Four patients were scanned with 18F-FDG, two with 18F-FDOPA, and two with 18F-FDA. Radiotracers were injected as previously described⁹, namely for 18F-FDG 370 MBq (60 minutes before acquisition), for 18F-FDOPA 444 MBq (30 minutes before acquisition), and for 18F-FDA 37 MBq (10 minutes before acquisition).

PET/CT acquisitions were performed on a 128-slice Biograph mCT scanner (Siemens Medical Solutions). Technical specifications and performance have been described.³⁰ This scanner's PET axial field of view (FOV) is 21.6 cm long. The CT settings were tube potential, 120 kV; tube current, 115 mA; and slice thickness, 1.5 mm. After completion of the PET/CT scan, patients were positioned on the PET/MR scanner promptly to preserve the remaining activity of the initial tracer injection. Patients were positioned in the PET/MR scanner similar to their positioning for the PET/CT examination.

PET/MR acquisition was performed on a Biograph mMR scanner (Siemens Medical Solutions) by one technologist from the Nuclear Medicine Division and one technologist from the MR Division. The Biograph mMR is a 3-Tesla whole-body MR scanner, with a concentric array of PET-detectors that allow for simultaneous PET and MR acquisitions. The detectors are made with avalanche photodiodes (APD). Technical specifications and the performance of the entire system have been described.³¹ This scanner's PET axial FOV is 25.8 cm long. Simultaneously to the PET acquisition, three MR sequences were acquired for each bed position (BP): a DIXON 3D T1-weighted MR sequence used for the generation of PET attenuation correction maps, and two axial T2-weighted sequences (a short TI inversion recovery (STIR) sequence (TR/TE, 4000/70 msec; flip angle 160°; slice thickness, 6 mm) and a half-Fourier acquired single-shot turbo spin-echo (HASTE) sequence (TR/TE, minimum/100 msec; flip angle 120°; slice thickness, 6 mm)), both used for anatomic allocation and delineation of lesions. All sequences were acquired without any contrast agent. The detailed imaging protocol is shown in Figure 1A.

All the PET image datasets (from PET/CT and from PET/MR) were reconstructed iteratively using an OSEM reconstruction algorithm. For PET/CT, PET attenuation correction was performed using attenuation maps based on low-dose, low energy CT images.³² For PET/MR, attenuation maps were generated on the basis of the 2-point DIXON MR imaging segmented and classified into four classes (air, lung, soft tissue, and fat), and then calculated on the basis of the presumed radiodensity of these tissue types, as previously described.³³ After reconstruction, images were displayed on a MedViewer viewing station (MedImage, Ann Harbor, MI).

Image analysis

Images were analyzed by two board-certified nuclear medicine readers and one board-certified radiologist reader. The image quality was assessed by noticing the presence of artifacts. Lesion detectability from PET data was also assessed (a lesion considered as detectable when lesion uptake is higher than its surrounding background uptake). For each PET-positive finding, the anatomic allocation and delineation allowed by the co-registered CT or MR method was assessed using a 4-point scale, as previously described.^{24,34} The ratings of each lesion were computed and expressed as mean $\pm$ SD.

RESULTS

Proceedings and Acquisition Times

The PET/MR acquisition was done immediately after the PET/CT, with a time interval (median; range) of 69; [56–112] min between the starting time of PET/CT and the starting time of PET/MR. The PET/CT and PET/MR acquisition starting times post-injection for each tracer is displayed in Figure 1B. Both PET/CT and PET/MR covered from the thighs to the head, except for one patient (#3) who required scanning from the feet to the head, due to widespread bone disease involving the extremities. For PET/CT, 6 to 7 BPs were required to cover the torso (10 for patient #3). This resulted in a total acquisition time (median; range) of 32.5; [18–42] min, depending on the size of the patient and the tracer used. For PET/MRI, 4 to 5 BPs were required to cover the torso (6 for patient #3). This resulted in a total acquisition time (median; range) of 31; [25–40] min, depending on the size of the patients and the tracer used. All patients were compliant, and scans were performed with no major concerns. The proceedings are shown in Table 2.

Assessment of PET images obtained from PET/MR compared to PET images obtained from PET/CT

With PET/MR we obtained good quality PET images. However, one of the 18F-FDG studies (patient #2) demonstrated an artifact on the PET images acquired from the PET/MR. It was characterized by a large photopenic region in the area of orthopedic hardware in the lumbar spine.

With PET/CT, a total of 53 PET-positive findings were evaluated. Lesions were located in the head-and-neck area (6), mediastinum (2), abdomen and pelvis (13), bones (26), liver (4), and lungs (2). Details of lesion locations for each patient are listed in Table 3. Of these 53 lesions, 51 were also observed with PET/MR (i.e., in the same subjects at an identical

location). Two bone lesions (an 8 mm located at the anterior L4 body vertebrae and a 6 mm located in the left transverse process of the upper sacrum that appeared weakly hypermetabolic on PET/CT, with an SUV max of 3.6 and 3.1, respectively) were missed on an 18F-FDA PET/MR scan (patient #8). Notably, in this same patient, two other bone lesions (right skull base, 8 mm, and left clavicle head, very small PET-positive focus with no measurable morphologic correlate) had poor tumor-to-background contrast on the PET data from PET/MR.

Assessment of anatomic allocation and delineation of PET-positive lesions

According to the 4-point-scale visual rating, reliable anatomic allocation and delineation of suspected PET-positive lesions were possible using low-dose CT (mean $\pm$ SD, 2.0 ± 0.9), STIR MR imaging (mean $\pm$ SD, 2.4 ± 0.9), and HASTE MR imaging (mean $\pm$ SD, 2.2 ± 0.9). Co-registered MR imaging (especially the STIR sequence) was equivalent to co-registered CT for mediastinal PGLs and bone and pulmonary metastases, and was superior to co-registered CT for head-and-neck PGLs, abdomino-pelvic PGLs, and liver metastases. The lesion rating for each modality and each location is displayed in Figure 2. A case with a head-and-neck tumor is presented in Figure 3.

A urinary bladder PGL (on an 18F-FDA study on patient #7) was not localized accurately by CT imaging because the urinary bladder was replenishing between the time of CT acquisition and the time of the PET acquisition. In contrast, fused PET/MR imaging showed correct alignment between the PET positive focus and its morphologic correlate (Figure 4).

For liver lesions, the non-contrast-enhanced low-dose CT dataset could allocate the PET-positive foci in the liver (on fused images PET foci were corresponding to liver tissue) but did not show any morphologic correlate. In contrast, non-CE T2-weighted MR datasets showed liver lesions with signal intensities higher than background. An example is presented in Figure 5.

One patient (#3) presented abundant non-pathological 18F-FDG uptake of activated brown adipose tissue in abdominal para-spinal and perinephric regions, and to a lesser extent in the cervical, supraclavicular, and thoracic sites. Co-registered CT and MR imaging were equivalent for identifying the non-pathological activated brown adipose tissue as the origin of this uptake.

DISCUSSION

In this study, we assessed the feasibility of integrated whole-body PET/MR to evaluate patients with PGLs using 18F-FDG, 18F-FDOPA, and 18F-FDA. The scan-duration, the quality of images, the detectability of the lesions, and the feasibility of anatomic allocation and delineation of the PET findings with co-registered anatomic images (i.e., CT or MR imaging) were assessed comparing PET/MR and PET/CT. We obtained good image quality in a reasonable acquisition time.

First, one early concern about PET/MR imaging was that workflows are time-consuming and complex and require scan protocols to be both time-efficient and comprehensive.²⁵ Due

to the integrated PET/MR scanner that allowed simultaneous acquisition of PET and MR data and the effective increase in the axial FOV for PET/MR—allowing the same distance to be covered with fewer BPs—our PET/MR studies were acquired in an acceptable acquisition time (maximum 40 min). They were tolerated by all patients with good compliance. In our PET/MR workflow, the co-registered MR sequences were acquired in less than five minutes per BP. In comparison, the PET acquisitions lasted five minutes per BP for 18F-FDG and eight minutes per BP for 18F-FDOPA and 18F-FDA. Therefore, the PET imaging portion was slightly longer than the MR imaging portion, representing the limiting factor regarding time requirement. Note that we chose to extend the acquisition time per BP for PET/MR (compared to the acquisition time per BP for PET/CT) to compensate for the radiotracer decay between the PET/CT and PET/MR acquisitions. When PET/MR is further validated for routine clinical use, we will be able to scan patients with PET/MR directly, without a previous PET/CT reference since the constraint of pre-scanning will no longer be necessary. It will allow us to use optimal uptake time and use acquisition times per BP for PET/MR that are not superior to those with PET/CT.

Integrated PET/MR provided PET data similar in quality to those obtained with PET/CT, despite the technical differences between PET/MR and PET/CT (the detectors made with APD in PET/MR compared to photomultipliers in PET/CT, and the approach used for attenuation correction). With one PET/MR imaging study, PET images showed artifacts next to the orthopedic hardware in the lumbar spine. The metallic orthopedic hardware created artifact in the MR DIXON images and altered the derived attenuation maps and the attenuation-corrected PET data. Such artifacts, due to metallic devices, have been reported.³⁵ This research finding should elicit caution when evaluating patients with orthopedic hardware; however, other methods for attenuation correction could be used.³⁶

Out of 53 PET-positive lesions found on PET/CT scans, 51 were also PET-positive on PET/MR scans. The two lesions that were missed on the PET data from the PET/MR were bone lesions from the same patient (scanned with 18F-FDA); however, these lesions had a low SUV on PET/CT (SUVmax 3.6). They were clearly identified on MR STIR images and showed high signal intensity compared to the normal bone around the lesion. Similarly, on the same patient, two other bone lesions—right base skull (8 mm) and left clavicle head (very small PET-positive focus with no morphologic correlate measurable)—had poor tumor-to-background contrast on the PET data from PET/MR when compared to the PET data from PET/CT. It is worth noting that for this patient, the PET/MR acquisition was delayed for technical reasons: it started 119 minutes after 18F-FDA injection compared to 10 minutes for PET/CT. Thus, a possible explanation could be that the lesions were subject to a “wash-out” process. The imperfect detection of bone lesions could also be explained by the limitation of the attenuation correction method regarding cortical bone representation (the DIXON-based segmentation method in our study for generating attenuation maps does not take bone tissue into account).^{37,38}

Co-registered MR imaging was superior for head-and-neck tumors, for lesions located in the abdomen and pelvis, and for liver metastases due to a better soft-tissue contrast. In the abdomen and pelvis, the peristalsis of the gastrointestinal tract and the urine bladder filling caused problems on side-by-side reading of PET and CT images acquired at different times.

For instance in our study, simultaneous PET/MR seemed to confer an advantage in the case of urinary bladder PGL. In the bone, the rating for anatomic allocation and delineation of PET-positive lesions was equivalent between PET/CT and PET/MR. However, MR imaging has been shown to have higher accuracy than CT for detection of bone metastases.³⁹ The non-superiority of PET/MR over PET/CT in our study for anatomic allocation and delineation of bone PET-positive lesions could be due to the fact that our co-registered MR sequences (STIR and HASTE) were in the axial plane with a 6 mm slice thickness. This might explain the imperfect detection of morphologic correlates concerning some small bone lesions.

In clinical practice, PET/MR imaging may be a valuable alternative to PET/CT because it can provide a better anatomic allocation and delineation of the PET findings, thanks to the MR imaging: it can evaluate for liver lesions before and after local treatment by radiofrequency ablation⁴⁰; it can evaluate for the detection of head-and-neck PGLs (before surgery or local treatment such as gamma-knife); and it can offer a better delineation of the lesions for a dosimetry study when a radiometabolic treatment is considered (131I-MIBG, 177Lu-octreotate, and 177Lu/90Y-DOTA-TATE/TOC/NOC).²⁸ Simultaneous PET/MR can also obtain an optimal temporal co-registration compared to PET/CT, which is essential for urinary bladder PGLs. Furthermore, its advantage over PET/CT regarding reduced radiation exposure is valuable, especially in children or young adults with familial PGL for whom close and prolonged follow-up studies are anticipated. Moreover, the co-registered CT in pediatric patients is sometimes of limited informative value due to children's body habitus (very little fat tissue) and to the low CT acquisition parameters (tube potential and current) that are implemented for reduction of radiation dose. Finally, PGL imaging is somewhat unique compared to the majority of other oncologic imaging because the distribution of tumors is truly distributed throughout the body. Thus, whole-body imaging is required for PGL staging, restaging, and follow-up. A key attribute of PET imaging is evaluation of the whole body. MR imaging is also necessary for accurate anatomic lesion delineation. However, whole-body scanning with MR imaging is not yet routine (typically, MR imaging has focused on a single body area, e.g., the abdomen). The protocols we have developed for PET/MR are able to rapidly provide whole body imaging. In this context, PET/MR could reduce the number of scanners required for patient management, shorten the overall scanning duration by doing both imaging exams at one time, and thus improve patient comfort and compliance.

In oncologic clinical research, new cancer hallmarks-specific PET radiopharmaceuticals (exploring proliferation, hypoxia, angiogenesis, apoptosis) and functional MR sequences (diffusion, dynamic contrast enhanced, spectroscopy) are widely used. They could also be very useful in PGL research since there is a need for improving PGL characterization and establishing new efficient treatment for PGL patients. To that aim, we can expect PET/MR to advance into a powerful dual-functional imaging tool that can simultaneously acquire new MR imaging sequences and PET with new tracers.

This study has some limitations. We only included eight patients who underwent PET/MR scans using one of the three different PET tracers. Because PET/CTs are done without an intravenous iodine contrast agent, we did not include intravenous gadolinium contrast-

enhanced sequences in our analysis in an attempt for a fair comparison. A more comprehensive protocol would address the evaluation of contrast-enhanced PET/MR in comparison to contrast-enhanced PET/CT.⁴¹

CONCLUSIONS

We have evaluated the feasibility of hybrid simultaneous whole-body PET/MR in 53 PGL or PGL-related lesions. We obtained high quality PET/MR imaging in a reasonable time. The detectability of lesions on PET images was good, although two bone lesions were not detectable on one 18F-FDA PET/MR scan, likely due to a wash-out of 18F-FDA. For lesion delineation, co-registered MR imaging tended to be superior to co-registered CT for head-and-neck tumors, for lesions located in the abdomen and pelvis, and for liver metastases. PET/MR could be particularly beneficial in the pediatric population and for precise lesion definition in organs in which MR offers better tissue contrast than CT. These encouraging results may form the foundation for future studies aiming to determine the diagnostic accuracy of PET/MR compared to PET/CT in PGLs.

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A. Imaging workflow

B. Acquisition starting times post-injection

Figure 1. Details on imaging workflow

A. Schematic display of the imaging workflow. CT was performed first, during a few seconds. Immediately after the CT, PET images were obtained, starting from the thighs and moving toward the head. The PET/CT axial field of view (FOV) is 21.6 cm. The acquisition times per BPs were 3 min for 18F-FDG, 5 min for 18F-FDOPA, and 6 min for 18F-FDA. After completion of the PET/CT scan, patients were subsequently positioned on the PET/MR scanner. In an attempt to compensate for the additional F-18 decay at the start of the PET/MR acquisitions, the time per BP was slightly increased: for patients injected with 18F-FDG, PET data were acquired in 5 minutes per BP; for patients injected with 18F-FDA,

PET data were acquired in 8 minutes per BP; and for patients injected with ^{18}F -FDOPA, PET data were acquired in 8 minutes per BP. Acquisition started from the thighs and moved toward the head. The PET/MR axial FOV is 25.8 cm. Simultaneously to the PET acquisition, for each BP, three MR sequences were acquired: a 2-point DIXON 3-dimensional volumetric interpolated breath-hold (VIBE) T1-weighted MR sequence, a Short TI inversion recovery sequence (STIR), and a Half-Fourier Acquired Single-shot Turbo spin Echo (HASTE). All sequences lasted together less than 5 minutes per BP.

B. PET/CT and PET/MR acquisition starting times post-injection, for each tracer, detailed for each patient.

Figure 2. Ratings of anatomic allocation of PET-positive findings using the co-registered (1) low-dose CT (in blue), (2) axial STIR sequence (in red), and (3) axial HASTE sequence (in green) for different lesion locations. Assessment was done using a 4-point scale, as previously described^{24,34}: 0, no anatomic correlation possible/no morphologic correlate detectable; 1, uncertain anatomic correlation/no morphologic correlate detectable; 2, good anatomic correlation/questionable morphologic correlate; and 3, excellent anatomic correlation with a clear morphologic correlate.

Figure 3.

18F-FDG PET/MR and PET/CT images in a 43-year-old female patient, with SDHD mutation, presenting with recurrence of a head-and-neck PGL in the right carotid bifurcation space, 18F-FDG avid. On PET/MR images, the axial T2-weighted STIR MR imaging (**A**) displays a hyperintense lesion, well delineated. Fusion of PET with MR imaging (**B** and **C**) confirms the anatomical co-localization of the uptake on PET images and the morphological lesion on MR imaging. In comparison, on PET/CT images (**D** and **E**), the CT dataset (**D**) shows a soft-tissue mass in the corresponding region, for which the outline is not precisely defined due to the poor lesion contrast over the local background.

Figure 4.

18F-FDA PET/MR and PET/CT images in a 66-year-old female patient presenting with a PGL lesion, localized to the posterior urinary bladder wall and bone metastatic lesions, 18F-FDA avid. Maximum intensity projection (MIP) images from PET/CT and PET/MR are displayed, respectively, on panel **A** and panel **B**. Axial cross-sectional PET/MR images (T2-weighted STIR MR imaging on panel **C** and fusion on panel **D**) allow visualization and delineation of the urinary bladder PGL, thanks to the hybrid imaging. Indeed, PET displays a pathologic focus of heterogeneous 18F-FDA uptake on the posterior right side of the urinary bladder that ‘merges’ with hyperactivity in the urinary bladder due to the radiotracer concentrating in the urine. MR imaging displays an isointense urinary bladder lesion that may be distinguished from the T2 hyperintense urine in the urinary bladder. Fusion of PET with MR imaging confirms the anatomical co-localization of the focal uptake in PET and the soft-tissue lesion in MR imaging. Focal uptake in the left anterior iliac bone lesion is clearly visualized on the two co-registered modalities.

Figure 5.

^{18}F -FDG PET/MR and PET/CT images in a 55-year-old male patient with SDHD mutation, presenting with a metastatic recurrence of a PGL with ^{18}F -FDG avid liver lesions. On PET/MR imaging, the axial T2-weighted STIR MR imaging (A) displays a hyperintense liver lesion, well delineated. Fusion of PET with MR imaging (B and C) confirms the anatomical co-localization of the uptake on PET images and the morphological lesion on MRI. In comparison, on PET/CT images (D and E), the CT dataset (D) does not show any morphologic correlate of the liver lesion. Fusion of PET with CT (E) allows anyway a good anatomic allocation of the focal uptake by localizing it in the liver.

Table 1

Patients clinical characteristics.

Patient #	Age (years)	Sex	Germline mutation	Initial date of PGL onset	Reason for evaluation at the time of MR/PET	Status at the time of MR/PET	Previous treatment (if applicable)	Tracer used for MR/PET
#1	43	F	SDHD	1987	Staging of recurrence	Primary	Surgery	18F-FDG
#2	50	F	SDHB	1984	Restaging	Metastatic	Surgery, chemotherapy, EBRT, 131I-MIBG	
#3	51	F	SDHB	2006	Restaging	Metastatic	Surgery, EBRT, 131I-MIBG	18F-FDOPA
#4	55	M	SDHD	1978	Restaging	Metastatic	Surgery, chemotherapy, EBRT, 131I-MIBG	
#5	34	M	Negative	2012	Initial staging	Primary	n/a	18F-FDA
#6	48	F	Negative	1979	Staging of recurrence	Metastatic	Surgery	
#7	66	F	Negative	1999	Restaging	Metastatic	Surgery, chemotherapy	18F-FDA
#8	48	F	MEN2	1989	Staging of recurrence	Metastatic	Surgery	

PGL: paraganglioma.

18F-FDG: 18F-fluorodeoxyglucose.

18F-FDOPA: 18F-fluorodihydroxyphenylalanine.

18F-FDA: 18F-fluorodopamine.

SDHB: Succinate dehydrogenase subunit B.

SDHD: Succinate dehydrogenase subunit D.

MEN2: Multiple endocrine neoplasia 2.

EBRT: External beam radiation therapy.

131I-MIBG: Iodine 131-MIBG radiometabolic therapy.

n/a: not applicable.

Table 2

Imaging times for PET/CT and PET/MR examinations.

Patient #	Radiotracer	PET/CT			PET/MRI		
		Time per BP	Number of BP	Total imaging time	Time per BP	Number of BP	Total imaging time
#1	18F-FDG	3 min	6	18 min	5 min	5	25 min
#2			7	21 min		5	25 min
#3			7+3	30 min		6	30 min
#4			6	18 min		5	25 min
#5	18F-FDOPA	5 min	7	35 min	8 min	5	40 min
#6			7	35 min		4	32 min
#7	18F-FDA	6 min	7	42 min	8 min	5	40 min
#8			7	42 min		5	40 min

The time per BP were fixed for each tracer. For PET/CT we followed our usual protocols. For PET/MR imaging, we voluntarily extended to compensate the lower activity due to decrease of radioactivity. The number of BP depended on the size of the patients. The PET covered from head to thighs (except patient #3 who was scanned from head to feet due to bone metastases in lower limbs). Fewer BP were needed for PET/MR compared to PET/CT due to the larger field of view of the PET/MR scanner.

BP: Bed position.

18F-FDG: 18F-fluorodeoxyglucose.

18F-FDOPA: 18F-fluorodihydroxyphenylalanine.

18F-FDA: 18F-fluorodopamine.

Table 3

Number and location of PET-positive lesions by patient.

Patient #	Tracer used	Primary lesions		Metastatic lesions			Total
		head-and-neck	Mediastinum	Abdomen and Pelvis	Bone	Liver	Lungs
#1	18F-FDG	2	0	0	0	0	0
#2		0	0	0	6	0	2
#3		0	0	1	6	0	0
#4		2	1	3	2	4	0
#5	18F-FDOPA	0	1	0	0	0	0
#6		0	0	2	0	0	0
#7	18F-FDA	0	0	3	6	0	0
#8		2	0	4	6*	0	0
TOTAL		6	2	13	26	4	2

18F-FDG: 18F-fluorodeoxyglucose.

18F-FDOPA: 18F-fluorodihydroxyphenylalanine.

18F-FDA: 18F-fluorodopamine.

* 2 bone lesions were missed on the PET data from PET/MR.