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# Clinical applications of PET/MR imaging: IRCCS San Raffaele Scientific Institute experience

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At IRCCS San Raffaele Scientific Institute, the research interests of the molecular imaging group are to provide technical capabilities and scientific expertise for integrating cutting-edge, multi-modality imaging into basic, translational and clinical research. Our research activity is particularly focused on the use of integrated molecular imaging modalities, including a very innovative fully hybrid PET/MR system, SIGNA™ PET/MR, with the use of different PET radiopharmaceuticals, for in vivo studies in different clinical settings.

In the evaluation of cancer patients, we utilize PET/MR for risk stratification and monitoring response to therapy. We have also investigated the clinical and the predictive/prognostic impact of integrated molecular imaging modalities in neoplasms and evaluated the development of innovative PET tracers for cancer. The aim of the research is the set-up of new non-invasive diagnostic imaging methods to be transferred into clinical practice to optimize diagnosis, prognosis and therapy in oncology.

PET/MR can have a significant impact on the diagnosis, staging and monitoring of soft-tissue cancers, particularly with the excellent soft-tissue imaging properties of MR. Our group has particularly studied the value of a fully integrated PET/MR in gynecological, prostate, pancreatic neuroendocrine tumors (NETs) and brain cancers. Here we present a summary of these findings and the value of PET/MR as a one-stop-shop modality.

## Endometrial cancer

In endometrial cancer (EC) patients, assessing deep myometrial invasion (MI) and lymph node (LN) involvement preoperatively is crucial. Surgical planning is typically based on information provided by biopsy (histotype, tumor grade) and morphological imaging-derived data (such as MI and LN involvement).

To date, MR imaging is considered the most accurate imaging technique for preoperative assessment of EC, due to its excellent soft-tissue contrast resolution. MR can accurately assess the depth of MI, which represents one of the most important morphological prognostic factors and can impact patient management by aiding in stratifying patients into low- versus intermediate-risk groups before surgery.[1-3]

PET with [$^{18}$F]fluoro-deoxyglucose ([$^{18}$F]FDG) is well-established in EC preoperative staging and is included in clinical guidelines for EC management.[4] Evaluation of deep MI and LN involvement, derived respectively from MR and PET studies in patients with EC, has shown to have good predictive value.[5,6] In these cases, the use of a fully integrated PET/MR offers the potential to merge the strengths of PET with the superior soft-tissue contrast resolution of MR, particularly in evaluating local tumor characteristics, such as the depth of myometrial invasion.[7]

In Ironi et al, we aimed to assess the diagnostic performance of hybrid [$^{18}$F]FDG PET/MR in EC staging, with a particular focus on MI and LN involvement detection.[8] PET/MR detected LN involvement

with high diagnostic accuracy (sensitivity [SN] of 0.8571, specificity [SP] of 0.9286, accuracy of 0.9143), and a high negative predictive value (NPV) for LN involvement (NPV of 0.9630, positive predictive value [PPV] of 0.7500). PET/MR detected all primary tumors and correctly staged 27 of the 36 women enrolled in the assessment of MI.

In general, most studies demonstrated an even detection rate between PET/MR and PET/CT. However, the possibility to merge PET and MR images using a hybrid modality such as PET/MR, complementing the single advantages of the two techniques, is definitely of value in patients with endometrial cancer.[8]

In our patient population, it has been demonstrated that a fully integrated PET/MR, such as SIGNA PET/MR, provides good to high accuracy in detecting MI and LN involvement. In addition, it has been shown that MR- and PET-derived parameters can predict the presence of lymphovascular space invasion (LVSI) and correctly stratify patients according to internationally accepted risk profiles. As demonstrated in this study, PET and MR provide a synergic role for predicting LVSI preoperatively, with MR also being predictive for the EC risk group, and might play a decisive role in planning therapeutic and surgical choice in view of personalized treatment approaches.[8]

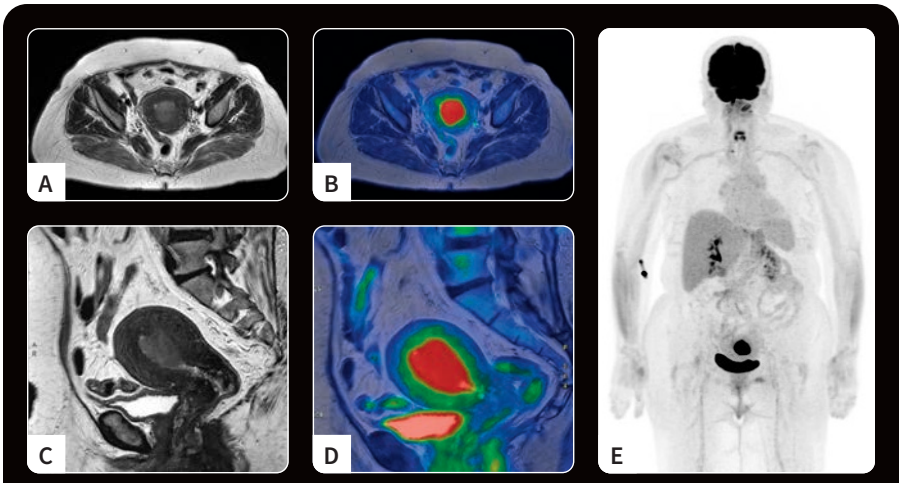


**Figure 1.** FDG PET/MR in endometrial cancer staging. (A, C) T2 PROPELLER (B, D) fused with PET. (E) Whole-body PET.

## Prostate cancer

It is well established that multiparametric MR (mpMRI) is a primary imaging modality for prostate cancer (PCa) assessment. It is commonly used to detect the primary tumor, guide biopsies and define the local extent of the disease. Its usefulness for local staging has been largely reported, although local staging with MR might be associated with limited sensitivity.[9]

The current EAU-ESTRO-SIOG guidelines report that PET/CT is a valuable imaging modality that might be considered in men with high-risk diseases undergoing initial staging. At diagnosis, whole-body staging for high-risk PCa patients is strongly recommended to identify those at risk of extracapsular extension, locally advanced disease and/or bone metastases.[10]

Prostate-specific membrane antigen (PSMA), a transmembrane protein with a significantly increased expression in PCa cells, can be used as an imaging biomarker and has been introduced in clinical practice for patient evaluation.

PET imaging using PSMA has gained significant attention in the clinical evaluation of PCa due to its superior sensitivity compared to conventional imaging and MR for detecting primary[11,12] and recurrent PCa[13,14], as well as LN involvement.[15-17]

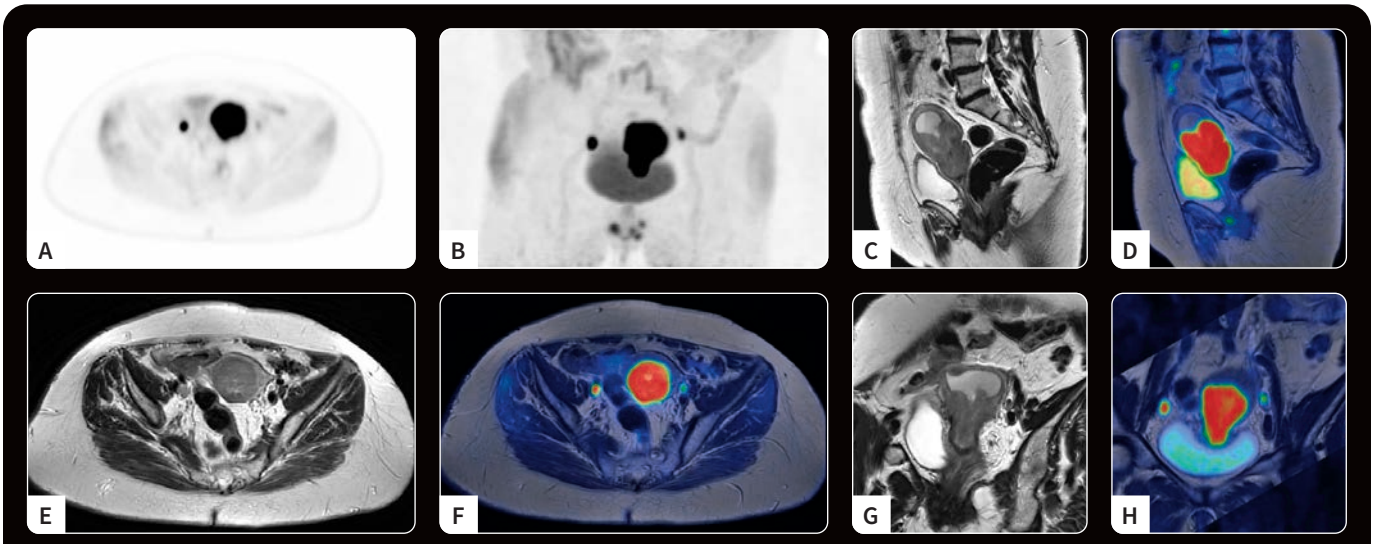


**Figure 2.** FDG PET/MR in endometrial cancer staging. (A, B) PET, (C, E, G) T2 PROPELLER MR and (D, F, H) T2 PROPELLER MR fused with PET demonstrate endometrial cancer and bilateral iliac LN involvement.

At IRCCS San Raffaele, we have investigated the clinical utility of PET/MR with [$^{68}$Ga]Ga-PSMA-11 both in high-risk PCa patients and in biochemically recurrent PCa.

In Mapelli 2021 et al.[18], [$^{68}$Ga]Ga-PSMA-11 detected intraprostatic lesions in all high-risk patients. Additionally, in two of the 22 patients, [$^{68}$Ga]Ga-PSMA-11 PET also detected seminal vesicle uptake. Whole-body [$^{68}$Ga]Ga-PSMA-11 images revealed suspicious LN involvement in seven of the 22 patients and bone involvement in three of the 22 patients. MR images showed intraprostatic disease in all patients, with 10 patients also presenting extracapsular extension (ECE) and seven patients presenting seminal vesicle invasion (SVI). Five out of 22 patients had pathologic pelvic LNs and one had bone lesions. One of the most relevant patient advantages we reported in this study is the potential to receive a diagnostic MR examination simultaneously to the PET image acquisition, thus obtaining all the necessary morphological and multiparametric information for accurate identification and characterization of the primary tumor. Acquiring a simultaneous PSMA-PET scan with the MR provides additional information regarding primary tumor characteristics, together with a whole-body evaluation of the disease. Further, the use of PET/MR reduces the radiation exposure for the patient.[18]

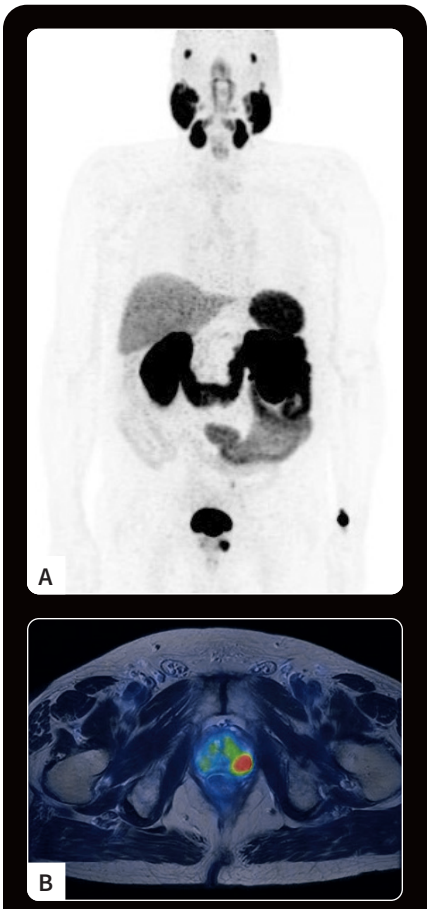


**Figure 3.** $^{68}$Ga-PSMA PET/MR in PCa staging. A 73-year-old man with biopsy proven PCa, Gleason score of 9 (5+4). PSA at the time of PET/MR was 6.4 ng/ml. (A) Whole-body PET and (B) axial fused PET/MR.

MR is expected to increase the diagnostic accuracy of PET imaging for local staging (ECE and SVI).[19] If used in combination with PET, MR could provide complementary information in the bone when PET findings are equivocal or when metastatic lesions do not show significant PSMA uptake. Whole-body MR could be of added value in monitoring the response to loco-regional or systemic treatments.

In addition, our research was also focused on the comparison of the value of PET/MR with the use of [$^{68}$Ga]Ga-PSMA-11 and with another PET tracer, [$^{68}$Ga]Ga-DOTA-RM2, a bombesin receptor antagonist with high affinity for gastrin-releasing peptide receptor (GRPR), that is also particularly promising as a PET imaging tool in PCa.[20]

Based on our results, we could demonstrate a potential complementary role of [$^{68}$Ga]Ga-PSMA-11 and [$^{68}$Ga]Ga-DOTA-RM2 in PCa staging in the clinical setting, with the possibility to identify different sites of disease by using a multitracer approach that might improve the disease characterization, which could ultimately have an impact on patient management and follow-up.[18]

We also conducted a systematic review and meta-analysis of the diagnostic accuracy obtained with PSMA PET/MR in patients with primary PCa. Ten papers with a sample size of at least 10 patients were included, three were retrospective and seven were prospective in design. All 10 studies (a total of 474 patients) had PET and MR images acquired simultaneously on a PET/MR system and had the main endpoint as the diagnostic accuracy of PSMA PET/MR in detecting primary prostate cancer. Seven studies used [$^{68}$Ga]Ga-PSMA-11 and the remaining three used a fluorine-labelled PSMA. In the qualitative analysis of each paper included in the meta-analysis, the authors suggest that the integrated PET/MR system demonstrated better sensitivity and diagnostic accuracy in detecting primary PCa compared to mpMRI and also to PET alone.[21]

Of particular relevance is the role of PSMA-PET as a complementary modality to mpMRI in primary prostate cancer localization for PI-RADS® 3 lesions. In local tumor staging, PET/MR provides an added possibility to predict extracapsular extension in patients with MR-occult prostate cancer compared to the use of PET/CT. PET/MR was also found to be very useful for local and regional disease, having almost equivalent performance in detecting bone and visceral metastases compared to PET/CT. The meta-analysis supports the promising role of the simultaneous acquisition of PSMA-PET and mpMRI for intraprostatic tumor detection in a whole-body, single-session

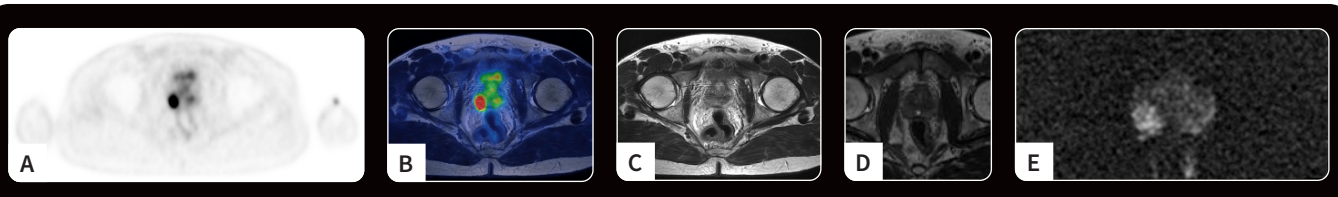


**Figure 4. A 53-year-old man with biopsy proven PCa, Gleason score of 9 (5+4) and PSA at diagnosis of 3.13 ng/mL. (A) Axial PET, (B) fused PET/MR, (C) T2 with large FOV, (D) T2 with small FOV and (E) DWI b1000 s/mm$^2$.**

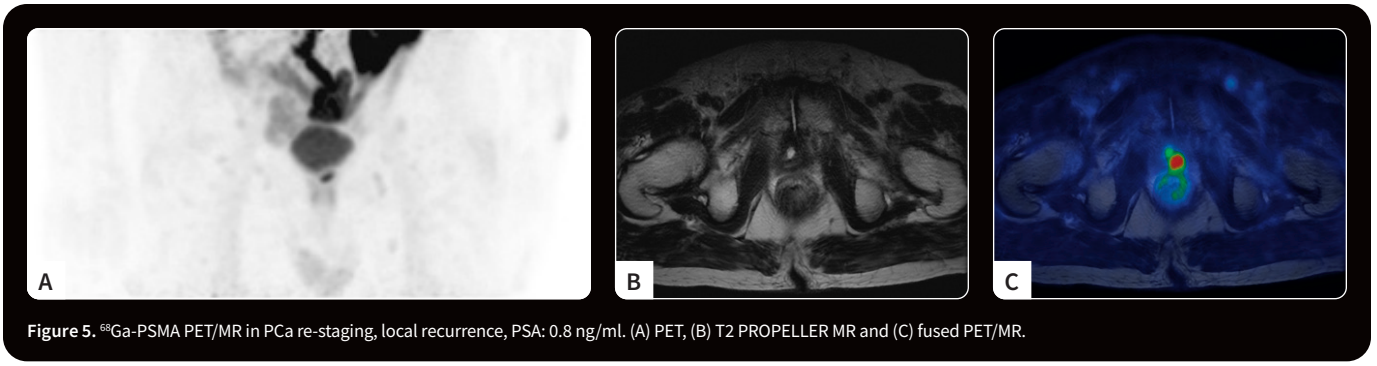


**Figure 5.** [68]Ga-PSMA PET/MR in PCa re-staging, local recurrence, PSA: 0.8 ng/ml. (A) PET, (B) T2 PROPELLER MR and (C) fused PET/MR.

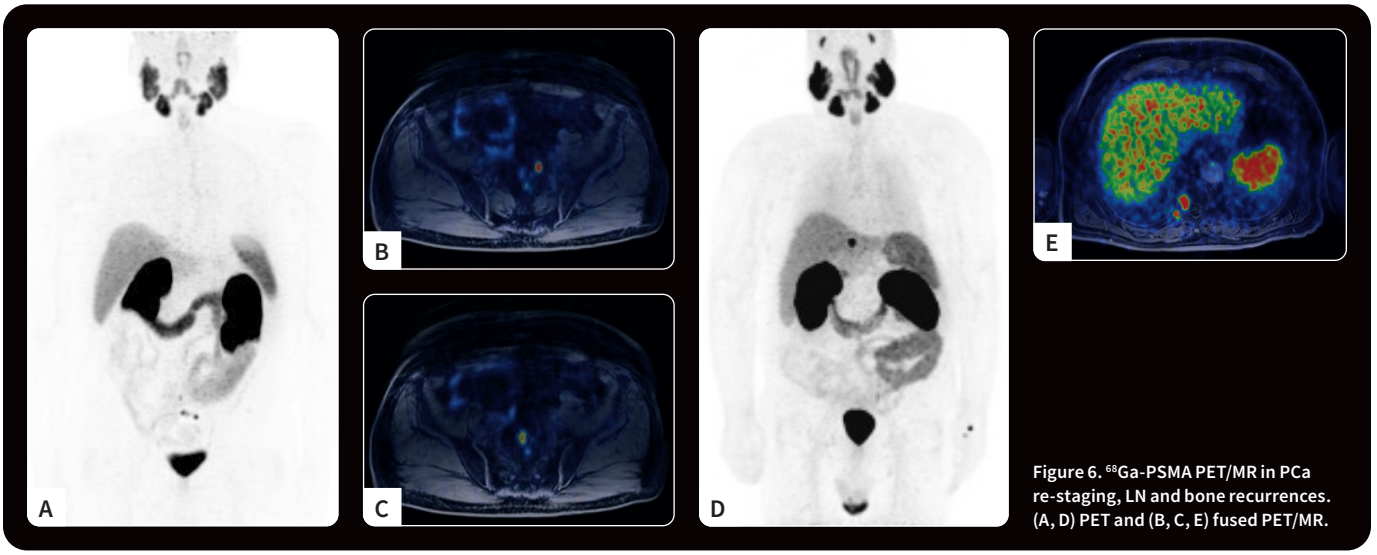


**Figure 6.** [68]Ga-PSMA PET/MR in PCa re-staging, LN and bone recurrences. (A, D) PET and (B, C, E) fused PET/MR.

examination. The simultaneous acquisition of PSMA-PET images and mpMRI provides metabolic, structural and functional information regarding PCa status.[21-27]

In Ghezzo et al,[13] we recently reported that in patients with biochemically recurrent PCa, combining MR with [68]Ga]Ga-PSMA-11 PET resulted in sensitivity of 100% and specificity of 69.2%, respectively. For mpMRI, sensitivity and specificity were 87.1% and 69.2%, respectively. In 35 patients with pathological findings from [68]Ga]Ga-PSMA-11 PET, 31 were confirmed as true positive by the composite reference standard. The nine patients classified as negative by integrated [68]Ga]Ga-PSMA-11 PET/MR were all confirmed as true negative at follow-up.[13]

The performance of [68]Ga]Ga-PSMA-11 PET for the detection of local recurrence was improved when combined with MR, while it was minimally effective for the detection of LN recurrence, in part due to the high sensitivity of [68]Ga]Ga-PSMA-11 PET.

In addition to the PET/MR benefits reported in Mapelli 2021 et al.[18], as noted above, morphological imaging with MR improves assessment of biochemical recurrent disease, considering that the determination of metastatic LNs is largely determined by size. The combination of PET and MR did not impact the performance of PET examinations in the other considered regions of recurrence.

A fully hybrid PET/MR paves the way to a completely innovative imaging approach for PCa recurrence with the simultaneous acquisition of PET and mpMRI for comprehensive (metabolic, structural and functional) imaging information regarding PCa status in a whole-body, single-session examination with better soft-tissue contrast and reduced radiation exposure.[21-27]

Radiomics is an emerging method of extracting features and quantitative metrics from medical images, and its role in PCa has been demonstrated.[28] Our group is particularly involved in this research field, and recently we evaluated the role of [68]Ga]Ga-PSMA-11 PET radiomics for the prediction of post-surgical International Society of Urological Pathology ($_{PS}$ISUP) grade in primary PCa. The results support the role of [68]Ga]Ga-PSMA-11 PET radiomics for the accurate and non-invasive prediction of $_{PS}$ISUP grade. ISUP grade at biopsy was upgraded in nine of 47 patients after prostatectomy, resulting in a bACC = 85.9%, SN = 71.9%, SP = 100%, PPV = 100% and NPV = 62.5%, while the best-performing radiomic model yielded a bACC = 87.6%, SN = 88.6%, SP = 86.7%, PPV = 94% and NPV = 82.5%.[29]

To establish an accurate correspondence between PET/MR findings and histology, facilitating a deeper understanding of PET tracer distribution and enabling advanced analyses like radiomics, we recently proposed a new and very robust workflow for co-registering prostate PET images from a dual-tracer PET/MR study with histopathological images of resected

prostate specimens. The method was optimized on images derived from patients who underwent both [$^{68}$Ga]Ga-PSMA-11 and [$^{68}$Ga]Ga-DOTA-RM2 PET/MR before radical prostatectomy. After surgery, in vivo PET/MR images were co-registered to histopathological images, by using ex vivo MR images of the specimen as an intermediate step. Markers were visible on both the histopathological images and on MR images. This approach that allows the quantitative assessment of dual-tracer PET/MR diagnostic accuracy at a millimetric scale might unveil radiotracer uptake mechanisms and identify new PET/MR biomarkers, thus establishing the basis for precision medicine and future analyses, such as radiomics.[30]

A new project for our group currently in progress is the evaluation of fully hybrid PET/MR with $^{18}$F-labelled PSMA and mpMRI as a one-stop approach for the diagnosis of clinically significant PCa. This prospective PET/MR evaluation could ideally reduce the number of false negative findings, while reducing the number of unnecessary prostate biopsies in patients with low-risk, clinically indolent PCa.

### Pancreas NET

PET imaging with $^{68}$Ga-DOTA-conjugated peptides is the standard functional imaging modality to study well-differentiated pancreatic neuroendocrine tumors (PanNETs) and is also included in the European guidelines.[31]

MR provides higher soft-tissue contrast compared to CT, along with functional imaging sequences including diffusion-weighted imaging (DWI). The consistent evidence for the superiority of PET/MR over PET/CT for detection of liver lesions has the potential to be clinically impactful by providing a more accurate number and distribution of liver metastases, influencing the choice between any combination of surgical, locoregional and systemic treatment options.[32]

As previously stated, radiomics is an emerging method for optimizing the extraction of information from medical images. In Mapelli et al,[33] we explored the potential to use imaging and radiomic parameters from [$^{68}$Ga]DOTATOC PET/MR imaging to predict histopathological prognostic factors in patients with PanNETs undergoing surgery.[33] PET/MR images were qualitatively and quantitatively interpreted: PET-derived $SUV_{max}$, $SUV_{mean}$, somatostatin receptor density (SRD), total lesion somatostatin receptor density (TLSRD), MR-derived apparent diffusion coefficient (ADC), arterial and late enhancement, necrosis, cystic degeneration and maximum diameter parameters were derived. Additionally, first- , second- and higher-order radiomic parameters were extracted from both PET and MR scans. The entire focal pathological [$^{68}$Ga]DOTATOC uptake corresponding to the primary tumor was manually segmented, slice-by-slice. The PET-derived volumes of interest (VOIs) and MR-derived VOIs (pre-contrast LAVA Flex T1-weighted and the axial T2-weighted PROPELLER MR sequences) were contoured and radiomic features were extracted. Next, we evaluated the correlation between [$^{68}$Ga]DOTATOC PET- and MR-derived imaging parameters and the tumors' histopathological prognostic factors, including grade, LN involvement and ratio between positive LNs using the nonparametric Spearman's correlation coefficient.

Based on ROC analyses, both $SUV_{max}$ and $SUV_{mean}$ resulted in good predictors of LN involvement. Specifically, $SUV_{max}$ showed an AUC of 0.850 (95% CI: 0.60–1.00), with an optimal cut-off value of 90.960 and correspondent SN and SP of 60% and 100%, respectively. Similarly, $SUV_{mean}$ showed an AUC of 0.783 (95% CI: 0.50–1.00), with an optimal cut-off value of 54.540 and correspondent sensitivity and specificity of 60% and 100%. Different correlations between radiomic features and grade, LN involvement and vascular invasion were identified. After adjustment for multiple comparisons, statistical significance held true exclusively for two original Gray Level Size Zone (GLSZM) texture features extracted from T2 MR sequences. Specifically, original glszm Gray Level Variance (GLV) and original GLSZM High Gray Level Zone Emphasis (HGLZE) both showed a significant, high, inverse correlation of -0.830 with LN involvement ($p < 0.005$, adjusted $p = 0.009$). The gold standard

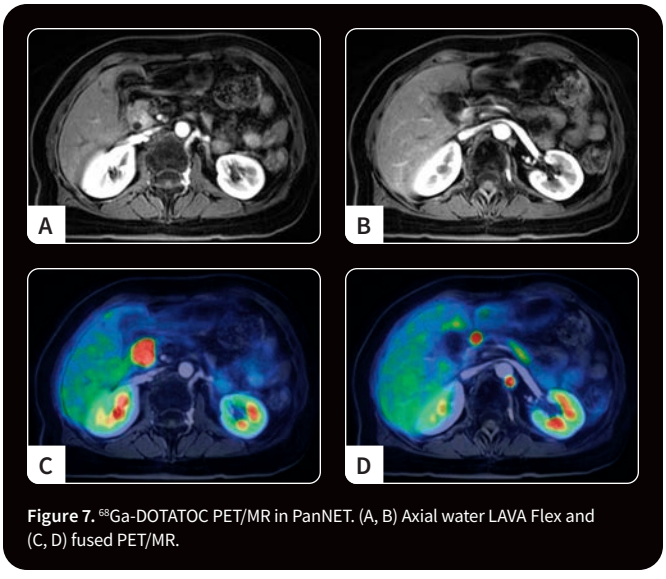


**Figure 7.** $^{68}$Ga-DOTATOC PET/MR in PanNET. (A, B) Axial water LAVA Flex and (C, D) fused PET/MR.

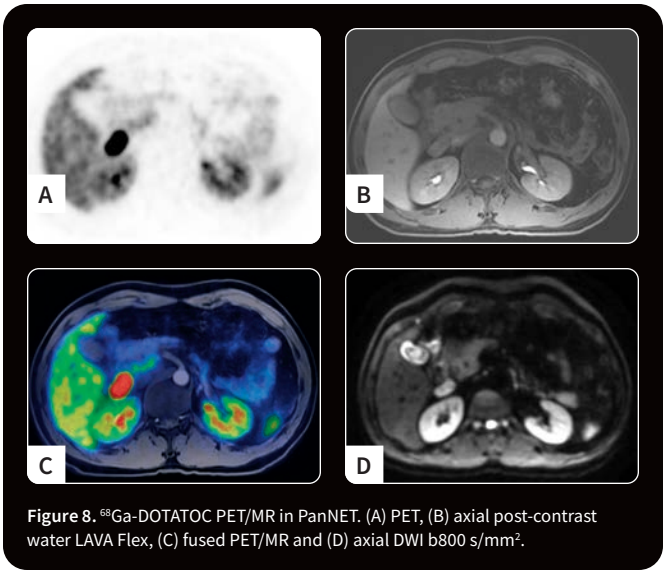


**Figure 8.** $^{68}$Ga-DOTATOC PET/MR in PanNET. (A) PET, (B) axial post-contrast water LAVA Flex, (C) fused PET/MR and (D) axial DWI b800 s/mm$^2$.

for our analysis was the histological examination, as all patients underwent surgery. In this study, we demonstrated the role of a fully hybrid PET/MR system for the synergic function of imaging parameters from the two modalities and highlighted the potential of imaging and radiomic parameters in assessing histopathological features of PanNET aggressiveness.[33]

Recently, we also demonstrated that imaging parameters derived from [$^{68}$Ga]DOTATOC PET have strong predictive value for DAXX/ATRX loss of expression in PanNETs, which represents a negative prognostic factor for patients with PanNETs.[34] Currently, radiological diameter, grade and Ki67 are the most reliable preoperative parameters associated to tumor aggressiveness, upon which choosing surgical intervention is based.

The results of the study showed that the information usually obtained from biopsy, such as grade and Ki67, combined with [$^{68}$Ga]DOTATOC PET parameters, including SRD, can be easily applied to clinical practice to estimate the probability of DAXX mutation in a more reliable way, thus supporting the clinical decision-making process.

The relevance of molecular imaging parameters, together with MR imaging with its high soft-tissue contrast, might be a valuable clinical one-stop-shop, whole-body imaging tool in neuroendocrine tumors.

### MotionFree Brain for pediatric neuro-oncology

In our institution, PET/MR is also applied to neuro-oncology studies with [$^{11}$C]Methionine (MET) and [$^{18}$F]fluoro-ethyl-tyrosine (FET) tracers. PET/MR imaging is particularly interesting in pediatric patients, as the simultaneous acquisition of two important examinations, such as PET and MR, avoid repeated sedations that are often required in this setting. In the context of pediatric neuro-oncology, we recently validated the use of a motion-correction tool for PET images.

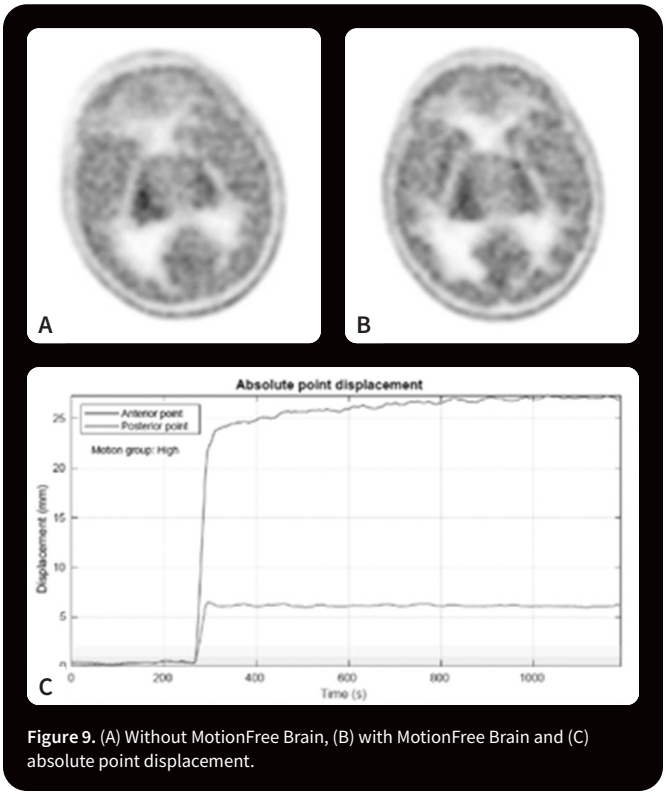


**Figure 9.** (A) Without MotionFree Brain, (B) with MotionFree Brain and (C) absolute point displacement.

Newer PET systems provide high spatial resolution, which is important for visualizing and characterizing biological processes in small structures, such as the brain. However, patient motion during the acquisition can impact PET reconstruction and affect the accuracy of SUV computations, as well as the qualitative image evaluation.

A prototype of a data-driven and retrospective approach to correct motion in brain PET imaging, MotionFree Brain, was tested at IRCCS San Raffaele in a cohort of [$^{11}$C]Methionine brain PET images of pediatric brain tumor patients studied on PET/MR.[35] We investigated the impact of MotionFree Brain both qualitatively and quantitatively in 27 pediatric patients with treated high-grade glioma. MRAC and zero time echo (ZTE) sequences were acquired during the 20-minute PET scan to generate attenuation correction maps. Additional diagnostic MR sequences were acquired before, during and after PET acquisition. All PET images were reconstructed using the same parameters with and without a prototype version of MotionFree Brain. The degree of motion was defined based on the median value of the displacement of two points of the head during the entire PET acquisition according to Spangler-Bickell et al.[35] The degree of motion was classified as "low" (<1 mm) for 18 patients, "medium" (between 1 and 2 mm) for five patients and "high" (>2 mm) for four patients. Twelve of the 27 patients had positive uptake, accounting for 16 lesions.

Qualitatively, no difference was shown in negative patients, while two lesions were more defined. Quantitatively, the mean percentage differences with the relative standard deviation for $SUV_{max}$, $SUV_{mean}$, $SUV_{peak}$ and MTV were: 2.66 ± 1.91%, 1.65 ± 1.71%, 2.77 ± 2.11%, and 13.32 ± 9.79%, respectively. Moreover, the difference in the PET parameters increased with the degree of motion of the patients. In conclusion, motion correction technology, such as MotionFree Brain, improves the quality of PET imaging and subsequent quantitative evaluation, such as $SUV_{mean}$.

### Conclusions

The clinical experience of PET/MR in IRCCS San Raffaele mainly includes gynecological, prostate cancers, neuroendocrine and brain tumors. These applications take advantage of the ability of the PET component with specific radiotracers in functionally characterizing neoplastic diseases, and of the MR component in providing superior soft-tissue resolution and offering synergistic information. The high soft-tissue and spatial resolution of MR is crucial for the evaluation of local tumor extent, while PET is superior at detecting nodal and distant metastatic disease. Furthermore, PET/MR systems such as SIGNA PET/MR are capable of providing potential prognostic insights and treatment response assessments.

The recent development of radiomic analysis, using classical statistics and modern machine learning algorithms to identify biomarkers based on multimodality imaging, have shown a great potential for treatment outcome prediction in different cancer entities. The simultaneous acquisition of PET and MR, offered by the hybrid PET/MR system, might facilitate a comprehensive imaging platform for feature extraction, with promising initial results.

**References:**


1. Colombo N, Creutzberg C, Amant F, et al. ESMO-ESGO-ESTRO Endometrial Consensus Conference Working Group. ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: diagnosis, treatment and follow-up. Ann Oncol. 2016 Jan;27(1):16-41. doi: 10.1093/annonc/mdv484.
2. Colombo N, Preti E, Landoni F, et al. ESMO Guidelines Working Group. Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013 Oct;24 Suppl 6:vi33-8. doi: 10.1093/annonc/mdt353.
3. Nougaret S, Reinhold C, Alsharif SS, et al. Endometrial Cancer: Combined MR Volumetry and Diffusion-weighted Imaging for Assessment of Myometrial and Lymphovascular Invasion and Tumor Grade. Radiology. 2015 Sep;276(3):797-808. doi: 10.1148/radiol.15141212.
4. Concin N, Matias-Guiu X, Vergote I, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. Int J Gynecol Cancer. 2021 Jan;31(1):12-39. doi: 10.1136/ijgc-2020-002230.
5. Crivellaro C, Landoni C, Elisei F, et al. Combining positron emission tomography/computed tomography, radiomics, and sentinel lymph node mapping for nodal staging of endometrial cancer patients. Int J Gynecol Cancer. 2020;30:378–382.
6. Mapelli P, Ironi G, Bergamini A, et al. Synergic role of preoperative 18F-fluorodeoxyglucose PET and MRI parameters in predicting histopathological features of endometrial cancer. Nucl Med Commun. 2020; 41:1073–1080.
7. Bezzi C, Zambella E, Ghezzo S, et al. 18F-FDG PET/MRI in endometrial cancer: systematic review and meta-analysis. Clin Transl Imaging 10, 45–58 (2022). https://doi.org/10.1007/s40336-021-00463-8.
8. Ironi G, Mapelli P, Bergamini A, et al. Hybrid PET/MRI in Staging Endometrial Cancer: Diagnostic and Predictive Value in a Prospective Cohort. Clin Nucl Med. 2022 Mar 1;47(3):e221-e229. doi: 10.1097/RLU.0000000000004064.
9. Wei JT, Barocas D, Carlsson S, et al. Early detection of prostate cancer: AUA/SUO guideline part 1: prostate cancer screening. J Urol. 2023;210(1):45-53.
10. Tilki D, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-ISUP-SIOG Guidelines on Prostate Cancer. Part II-2024 Update: Treatment of Relapsing and Metastatic Prostate Cancer. Eur Urol. 2024 Aug;86(2):164-182. doi: 10.1016/j.eururo.2024.04.010.
11. Emmett L, Buteau J, Papa N, et al. The Additive Diagnostic Value of Prostate-specific Membrane Antigen Positron Emission Tomography Computed Tomography to Multiparametric Magnetic Resonance Imaging Triage in the Diagnosis of Prostate Cancer (PRIMARY): A Prospective Multicentre Study. Eur Urol. 2021 Dec;80(6):682-689. doi: 10.1016/j.eururo.2021.08.002.
12. Ferraro DA, Becker AS, Kranzbühler B, et al. Diagnostic performance of 68Ga-PSMA-11 PET/MRI-guided biopsy in patients with suspected prostate cancer: a prospective single-center study. Eur J Nucl Med Mol Imaging. 2021 Sep;48(10):3315-3324. doi: 10.1007/s00259-021-05261-y.
13. Ghezzo S, Mapelli P, Samanes Gajate AM, et al. Diagnostic accuracy of fully hybrid [68Ga]Ga-PSMA-11 PET/MRI and [68Ga]Ga-RM2 PET/MRI in patients with biochemically recurrent prostate cancer: a prospective single-center phase II clinical trial. Eur J Nucl Med Mol Imaging. 2024 Feb;51(3):907-918. doi: 10.1007/s00259-023-06483-y.
14. Fendler WP, Calais J, Eiber M, et al. Assessment of 68Ga-PSMA-11 PET Accuracy in Localizing Recurrent Prostate Cancer: A Prospective Single-Arm Clinical Trial. JAMA Oncol. 2019 Jun 1;5(6):856-863. doi: 10.1001/jamaoncol.2019.0096.
15. Morris MJ, Rowe SP, Gorin MA, et al. CONDOR Study Group. Diagnostic Performance of 18F-DCFPyL-PET/CT in Men with Biochemically Recurrent Prostate Cancer: Results from the CONDOR Phase III, Multicenter Study. Clin Cancer Res. 2021 Jul 1;27(13):3674-3682. doi: 10.1158/1078-0432.CCR-20-4573. Epub 2021 Feb 23.
16. Hofman MS, Lawrentschuk N, Francis RJ, et al. proPSMA Study Group Collaborators. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. Lancet. 2020 Apr 11;395(10231):1208-1216. doi: 10.1016/S0140-6736(20)30314-7. Epub 2020 Mar 22.
17. Petersen LJ, Zacho HD. PSMA PET for primary lymph node staging of intermediate and high-risk prostate cancer: an expedited systematic review. Cancer Imaging. 2020 Jan 23;20(1):10. doi: 10.1186/s40644-020-0290-9.
18. Mapelli P, Ghezzo S, Samanes Gajate AM, et al. Preliminary Results of an Ongoing Prospective Clinical Trial on the Use of 68Ga-PSMA and 68Ga-DOTA-RM2 PET/MRI in Staging of High-Risk Prostate Cancer Patients. Diagnostics (Basel). 2021 Nov 9;11(11):2068. doi: 10.3390/diagnostics11112068.
19. Muehlematter UJ, Burger IA, Becker AS, et al. Diagnostic Accuracy of Multiparametric MRI versus (68)Ga-PSMA-11 PET/MRI for Extracapsular Extension and Seminal Vesicle Invasion in Patients with Prostate Cancer. Radiology. 2019 Nov;293(2):350-358. doi: 10.1148/radiol.2019190687. Epub 2019 Sep 10.
20. Körner M, Waser B, Rehmann R, et al. Early over-expression of GRP receptors in prostatic carcinogenesis. Prostate. 2014 Feb;74(2):217-24. doi: 10.1002/pros.22743. Epub 2013 Oct 22.
21. Mapelli P, Ghezzo S, Spataro A, et al. Systematic Review and Metanalysis on the Role of Prostate-Specific Membrane Antigen Positron Emission Tomography/Magnetic Resonance Imaging for Intraprostatic Tumour Assessment. Magn Reson Imaging Clin N Am. 2023 Nov;31(4):605-611. doi: 10.1016/j.mric.2023.06.006. Epub 2023 Aug 3.
22. Hicks RM, Simko JP, Westphalen AC, et al. Diagnostic Accuracy of 68Ga-PSMA-11 PET/MRI Compared with Multiparametric MRI in the Detection of Prostate Cancer. Radiology. 2018 Dec;289(3):730-737. doi: 10.1148/radiol.2018180788. Epub 2018 Sep 18.
23. Metser U, Ortega C, Perlis N, et al. Detection of clinically significant prostate cancer with 18F-DCFPyL PET/multiparametric MR. Eur J Nucl Med Mol Imaging. 2021 Oct;48(11):3702-3711. doi: 10.1007/s00259-021-05355-7. Epub 2021 Apr 12.
24. Bodar YJL, Zwezerijnen BGJC, van der Voorn PJ, et al. Prospective analysis of clinically significant prostate cancer detection with [18F]DCFPyL PET/MRI compared to multiparametric MRI: a comparison with the histopathology in the radical prostatectomy specimen, the ProStaPET study. Eur J Nucl Med Mol Imaging. 2022 Apr;49(5):1731-1742. doi: 10.1007/s00259-021-05604-9. Epub 2021 Nov 2.
25. Zeng Y, Leng X, Liao H, et al. Diagnostic value of integrated 18F-PSMA-1007 PET/MRI compared with that of biparametric MRI for the detection of prostate cancer. Prostate Int. 2022 Jun;10(2):108-116. doi: 10.1016/j.prnil.2022.03.003. Epub 2022 Mar 28.
26. Margel D, Bernstine H, Groshar D, et al. Diagnostic Performance of 68Ga Prostate-specific Membrane Antigen PET/MRI Compared with Multiparametric MRI for Detecting Clinically Significant Prostate Cancer. Radiology. 2021 Nov;301(2):379-386. doi: 10.1148/radiol.2021204093. Epub 2021 Aug 31.
27. Eiber M, Weirich G, Holzapfel K, et al. Simultaneous 68Ga-PSMA HBED-CC PET/MRI Improves the Localization of Primary Prostate Cancer. Eur Urol. 2016 Nov;70(5):829-836. doi: 10.1016/j.eururo.2015.12.053. Epub 2016 Jan 18.
28. Ghezzo S, Bezzi C, Presotto L, et al. State of the art of radiomic analysis in the clinical management of prostate cancer: A systematic review. Crit Rev Oncol Hematol. 2022 Jan;169:103544. doi: 10.1016/j.critrevonc.2021.103544. Epub 2021 Nov 18.
29. Ghezzo S, Mapelli P, Bezzi C, et al. Role of [68Ga]Ga-PSMA-11 PET radiomics to predict post-surgical ISUP grade in primary prostate cancer. Eur J Nucl Med Mol Imaging. 2023 Jul;50(8):2548-2560. doi: 10.1007/s00259-023-06187-3. Epub 2023 Mar 18.
30. Ghezzo S, Neri I, Mapelli P, et al. [68Ga]Ga-PSMA and [68Ga]Ga-RM2 PET/MRI vs. Histopathological Images in Prostate Cancer: A New Workflow for Spatial Co-Registration. Bioengineering (Basel). 2023 Aug 11;10(8):953. doi: 10.3390/bioengineering10080953.
31. Bozkurt MF, Virgolini I, Balogova S, et al. Guideline for PET/CT imaging of neuroendocrine neoplasms with 68Ga-DOTA-conjugated somatostatin receptor targeting peptides and 18F-DOPA. Eur J Nucl Med Mol Imaging. 2017 Aug;44(9):1588-1601. doi: 10.1007/s00259-017-3728-y. Epub 2017 May 25.
32. Pirasteh A Riedl C, Mayerhoefer ME et al. PET/MRI for neuroendocrine tumors: a match made in heaven or just another hype? Clin Transl Imaging. 2019 Dec;7(6):405-413. doi: 10.1007/s40336-019-00344-1. Epub 2019 Sep 20.
33. Mapelli P, Bezzi C, Palumbo D, et al. 68Ga-DOTATOC PET/MR imaging and radiomic parameters in predicting histopathological prognostic factors in patients with pancreatic neuroendocrine well-differentiated tumours. Eur J Nucl Med Mol Imaging. 2022 Jun;49(7):2352-2363. doi: 10.1007/s00259-022-05677-0. Epub 2022 Feb 14.
34. Mapelli P, Bezzi C, Muffatti F, et al. Somatostatin receptor activity assessed by 68Ga-DOTATOC PET can preoperatively predict DAXX/ATRX loss of expression in well-differentiated pancreatic neuroendocrine tumors. Eur J Nucl Med Mol Imaging. 2023 Jul;50(9):2818-2829. doi: 10.1007/s00259-023-06210-7. Epub 2023 Apr 3.
35. Spangler-Bickell MG, Hurley SA, Pirasteh A, et al. Evaluation of Data-Driven Rigid Motion Correction in Clinical Brain PET. Imaging. J Nucl Med. 2022 Oct;63(10):1604-1610. doi: 10.2967/jnumed.121.263309.