

## **<sup>18</sup>F-FDG PET/MRI with DWI: one-stop shop for paediatric sarcomas**

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## Aims and objectives

Sarcomas are heterogeneous tumor accounting for nearly 20% of all pediatric solid malignancies. The vast majority are soft tissue sarcomas, while malignant bone neoplasms account for around 10% [1]. The diagnostic and therapeutic management of pediatric sarcomas is complex and requires a multidisciplinary approach. MRI is considered the main imaging technique for primary tumor assessment and for local recurrences detection while systemic staging is mostly based on Computed Tomography (CT) and Positron Emission Tomography/CT (PET/CT) [2].

Combining the benefits of morphological and high soft tissue contrast imaging of MR and the metabolic information of PET, integrated PET/MRI is an innovative and highly promising diagnostic tool in oncological imaging. Several studies have already shown very good results about the application of  $^{18}\text{F}$ -FDG PET/MRI, with and without DWI, for lymphoma, pulmonary neoplasms, rectal cancer, breast neoplasms and for sarcomas in adults. [3-7]

Despite the intrinsic advantage of a low radiation dose than other whole-body techniques (e.g., PET/CT) and the excellent results already obtained in pediatric oncologic imaging [8], to the best of our knowledge, the role of PET/MRI for pediatric sarcomas was not assessed yet. Therefore, our aim was to investigate the diagnostic performance of  $^{18}\text{F}$ -FDG PET/MRI, including DWI, for pediatric sarcomas at staging and restaging.

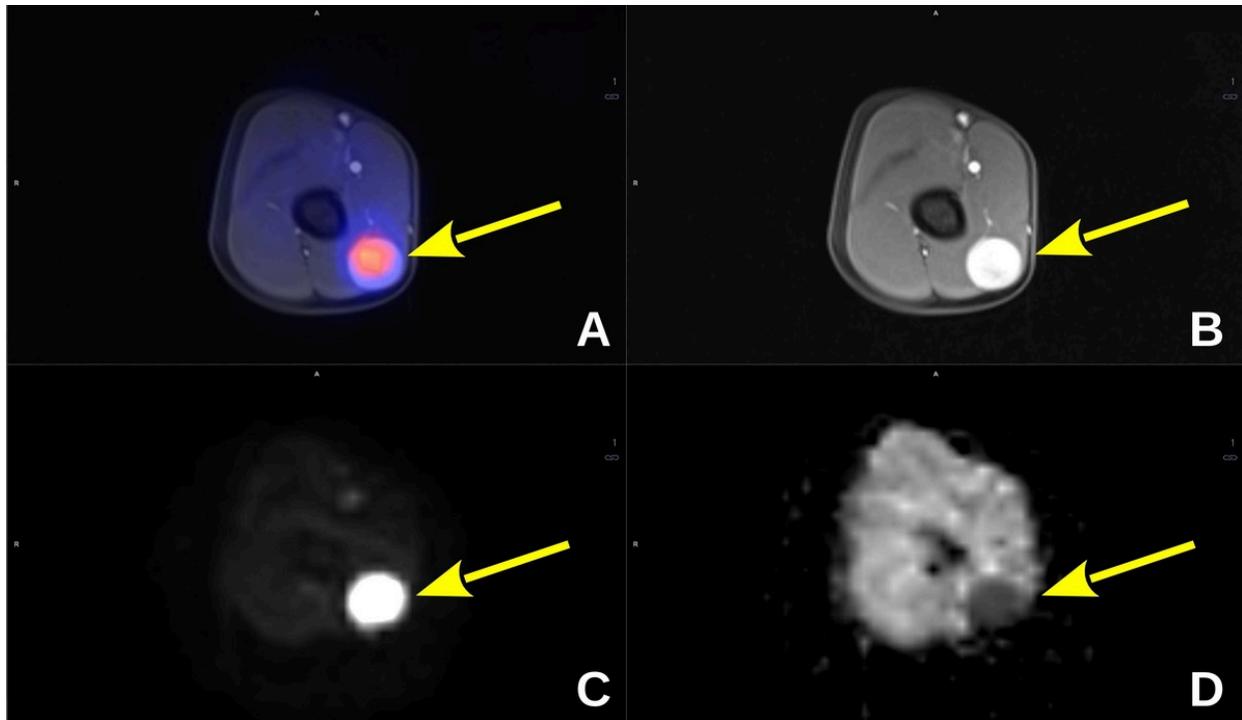
## Methods and materials

Pediatric patients with histologically proven sarcoma who underwent  $^{18}\text{F}$ -FDG PET/MRI (i.e., fully-integrated) for initial staging or re-staging were included in this retrospective study. The MRI protocol of the PET/MR scan had to include at least the following sequences: axial Turbo Inversion Recovery Magnitude (TIRM), axial Half-Fourier Acquisition Single-shot Turbo spin Echo imaging (HASTE), coronal T1w Turbo Spin Echo (TSE), pre-contrast and contrast enhanced axial Volumetric Interpolated Breath-hold Examination (VIBE) and axial whole body Diffusion Weighted Imaging (DWI). Each examination was evaluated independently and then in consensus by two teams, each composed by one radiologist and one nuclear medicine physician; all raters were blinded to the clinical information and to conventional imaging results. Each team assessed the presence of primary tumor, local and distant nodal involvement, skeletal and pulmonary metastases as well as metastatic lesions in any other organ/system. A maximum of six lesions per investigated region was recorded. PET/MRI was rated positive if at least two of the following criteria were satisfied: 1) focal pathologic uptake at PET; 2) morphological correlate at any MR sequence (excluding DWI); 3) restricted diffusion at DWI. Cohen's Kappa coefficient ( $\kappa$ ) was used to investigate the inter-observer agreement between the two teams. PET/MRI sensitivity and specificity were calculated considering histological examination and conventional imaging as reference standard (i.e., MRI of the area affected by the primary tumor for local staging and whole body contrast enhanced CT for the detection of distant metastases).

## Results

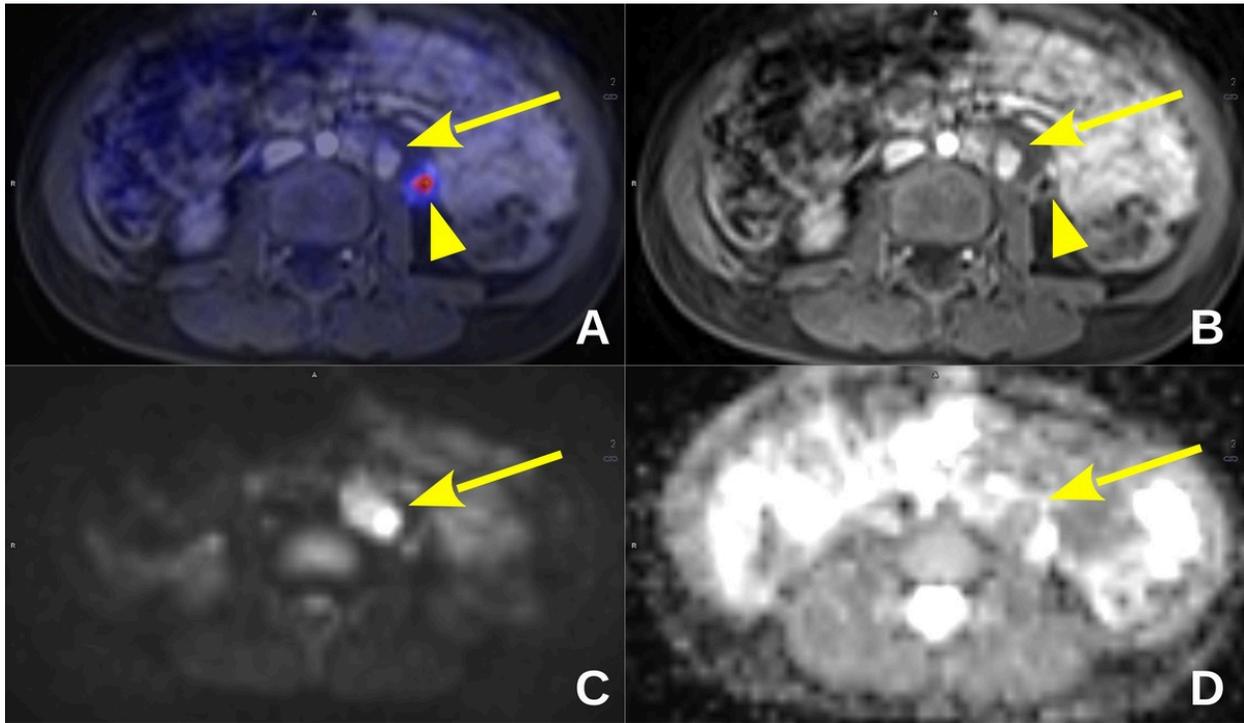
Sixteen patients met the inclusion criteria (nine males, seven females; mean age  $8.8 \pm 4.9$  years). Histology revealed nine rhabdomyosarcoma, two Ewing-sarcoma, diffuse myofibromatosis, chondroblastic osteosarcoma, angiosarcoma, extrarenal-rhabdoid tumor and undifferentiated sarcoma one each. The overall inter-observer agreement between the two teams turned out to be very high ( $\kappa=0.994$ ). Discordant results emerged only for the detection of a local lymph node in a patient affected by a rhabdoid-tumor and for two peritoneal metastases in a patient with angiosarcoma. When compared to the reference standard, PET/MRI showed 100% specificity for the diagnosis of the primary tumor (Fig. 1), recurrence, and also for the detection of nodal and distant metastases. One primary lesion (i.e., mediastinal rhabdomyosarcoma) was missed at restaging ( $\text{Sensitivity}_{\text{primary}}=93.3\%$ ) since it met only the morphological MRI criteria without showing any pathologic uptake at PET or restricted diffusion at DWI. On the contrary, two recurrences (i.e., respectively one rhabdomyosarcoma and one extra-renal rhabdoid tumor) were correctly diagnosed, despite the absence of pathologic glycolytic activity, because of the pathologic morphologic features at MRI and the restricted diffusion at DWI (Fig. 2). No local or distant nodal lesions were missed at PET/MR ( $\text{Sensitivity}_{\text{local\_nodal}}=100\%$ ;  $\text{Sensitivity}_{\text{distant\_nodal}}=100\%$ ). Regarding the detection of distant metastases, two pulmonary (i.e., two patients respectively affected by rhabdomyosarcoma and undifferentiated sarcoma) and six bone metastases (i.e., all in one patient with rhabdomyosarcoma examined after treatment) were not detected at PET/MRI ( $\text{Sensitivity}_{\text{lung}}=50\%$ ;  $\text{Sensitivity}_{\text{skeletal}}=75\%$ ). All other metastatic lesions affecting different sites than the above-mentioned ones (e.g., intramuscular, intraperitoneal, and mediastinal metastases) were correctly diagnosed ( $\text{Sensitivity}_{\text{meta\_others}}=100\%$ ) (Fig. 3). Overall, PET/MRI showed 90.9% sensitivity and 100% specificity for pediatric sarcomas.

**Images for this section:**



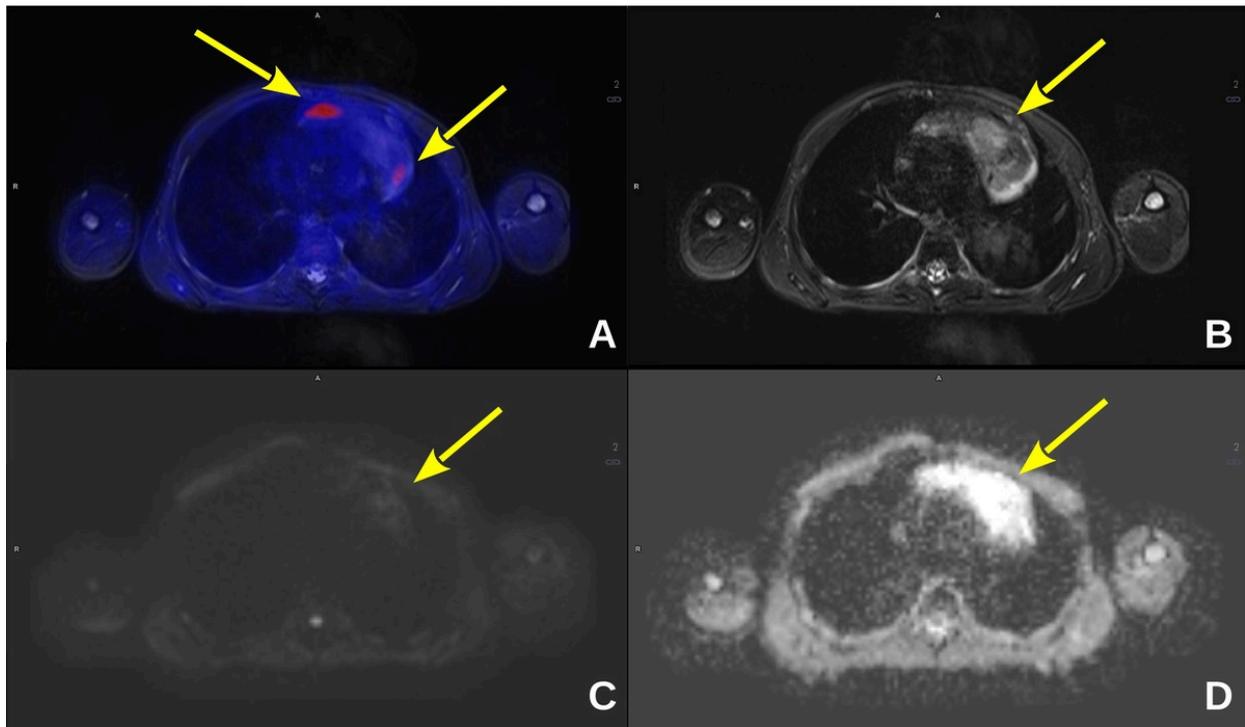
**Fig. 1:** Ten-year-old girl with rhabdomyosarcoma of the right biceps brachii (yellow arrows in A, B, C and D) examined at [18F]-FDG PET/MRI for staging. The primary tumor demonstrated pathologic uptake (fused PET/MR image in A), strong contrast enhancement (B) and restricted diffusion (1000 b value in C and ADC map in D) at PET/MRI.

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**Fig. 2:** Five-year-old girl with recurrent extrarenal rhabdoid tumor (yellow arrows in A, B, C and D). The retroperitoneal lesion was correctly diagnosed at PET/MRI, despite the absence of uptake (A) because of the pathologic feature at MR (strong contrast enhancement, yellow arrow in B), and restricted diffusion at DWI (yellow arrow in C and D). The hyperintense spot close to the neoplastic mass in the fused PET/MR image in A (yellow arrowhead) is the left ureter containing  $[^{18}\text{F}]\text{-FDG}$  marked urine.

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**Fig. 3:** Eleven-year-old boy with a metastatic rhabdomyosarcoma of the left gluteus maximus scanned at [18F]-FDG PET/MRI for restaging. A heterogeneous mediastinal mass (yellow arrows in A, B, C and D) demonstrating pathologic uptake at PET (yellow arrows on the fused PET/MR image in A), slight and inhomogenous hyperintensity on axial TIRM (B) but no restricted diffusion (b1000 image and ADC map in C and D). The lesion was considered positive at PET/MRI because it met two out of three diagnostic criteria.

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## Conclusion

Our preliminary results demonstrated that  $^{18}\text{F}$ -FDG PET/MRI with whole body DWI guarantees an excellent reliability and a high diagnostic performance for pediatric sarcomas. Therefore, considering also its low dose radiation exposure, PET/MRI should be taken into account as one-stop shop for pediatric sarcomas at staging and restaging. Further studies on a larger population are necessary not only to improve pulmonary MR imaging and thus increase the detection of lung metastases but also to fully assess the overall role of PET/MRI for pediatric sarcomas.

## Personal information

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