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# Imaging Capabilities of the IRIS and IRIS XL-260 PET/CT Systems for High-Throughput Imaging: a Quantification Cross Validation Study

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**Abstract**—The concept of imaging several subjects simultaneously is an active preclinical research topic. In the present paper, we assessed the imaging capabilities of two PET/CT systems based on similar detector technology. The IRIS system is a mice/rat imaging system arranged in two rings of eight detectors each, the more recent IRIS XL 260, dedicated to Non-Human Primate (NHP) imaging has a single ring of sixteen detectors. Both systems were equipped with standard animal cells (Minerve) and 3-mice adapters. Our objective is to study which of these systems could be more appropriate to perform quantitative high-throughput imaging on mice. Phantoms and [<sup>18</sup>F]FDG tumor-bearing mice acquisitions have been conducted in single and high-throughput modes using both the IRIS (up to 3 mice) and the IRIS XL-260 PET/CT (up to 6 mice) systems.

Image Quality Phantom results obtained in high-throughput mode show some slight degradation of the recovery coefficient for rods of 1, 2 and 3 mm in diameter compared to the single-mode results, as one would normally expect. Similarly, we observed a decrease in image uniformity between the single- and the high-throughput modes for both the IRIS PET and the IRIS XL-260 PET systems. We performed [<sup>18</sup>F]FDG tumor-bearing mice PET acquisitions with both systems. In order to estimate the quantification differences in all the studied configurations, we calculate the ratios between the %ID/g values extracted from the PET images and the ex-vivo values. In single mode acquisitions, ratios of  $0.94 \pm 0.09$  and  $0.83 \pm 0.08$  were obtained for the IRIS and the IRIS XL-260 PET systems, respectively. In high-throughput mode, ratios of  $0.78 \pm 0.12$  and  $0.73 \pm 0.13$  were obtained for the IRIS and the IRIS XL-260 PET systems, respectively. The difference in %ID/g between static acquisitions and ex-vivo value is not statistically significant (p-value > 0.1) for both PET systems in single mode, as well as for the IRIS system in high-throughput mode. We noted a slightly higher statistical difference between static acquisitions and ex-vivo values for the IRIS XL-260 system with a p-value of 0.015.

Phantoms and in-vivo studies have made it possible to highlight the capability of the two systems to perform high-throughput acquisitions. Our results suggest that the IRIS system configuration may be the most suitable when aiming for quantitative high-throughput mice imaging. The large transverse field of view of the IRIS XL-260 makes it possible to image a greater number of mice simultaneously, which may be useful in specific cases, such as studies using an expensive radiotracer and/or with a short half-life. However, the IRIS PET/CT offers a full axial coverage of the animals and a higher sensitivity.

## I. INTRODUCTION

In preclinical emission tomography imaging, several research groups have recently proposed to image several mice simultaneously mainly to reduce the costs and to increase the throughput. Simultaneous scanning of several animals also ensures injections with the

This work involved human subjects or animals in its research. Approval of all ethical and experimental procedures and protocols was granted by the Alsace Regional Ethics Committee for Animal Experimentation under Application APAFIS#15255, and performed in line with the European Institutes of Health Guidelines.

All authors declare that they have no known conflicts of interest in terms of competing financial interests or personal relationships that could have an influence or are relevant to the work reported in this paper.

same specific activity, which may be otherwise subject to significant variations when animals are injected at different times and possibly with tracers from different production batches. However, scanning two (or more) animals comes with some downsides such as an increased attenuation, dead-time and rates of scatter and random events [1], [2]. In addition, it is well known that the performance of a Positron Emission Tomograph (PET) system, in terms of spatial resolution and sensitivity, is optimal at the center of the field of view (FOV) and degrades quickly with increasing distance from the center.

Wolf *et al* and Aide *et al* studied the possibility to scan several small rodents using clinical PET associated with a Computed Tomograph (CT) systems [3], [4]. Clinical PET scanners have a limited spatial resolution as compared to small-animal PET scanners. However, Aide *et al* demonstrated the feasibility of scanning multiple animals with a clinical PET scanner using advanced reconstruction algorithms that include a spatially variant spatial resolution model [4]. Previous studies on simultaneous scanning of multiple animals have also been published using small-animal PET scanners. Siepel *et al* investigated the effect of scanning four mice simultaneously on image quality [1]. The same year, Aide *et al* first evaluated the feasibility to scan four mice simultaneously using the Inveon PET scanner [5]. This study assessed spatial resolution and scatter measurements as well as image quality using the Image Quality Phantom (IQP), and tumor bearing mice imaged in groups of four but did not report on the uniformity behavior. A few years later, Habte *et al* investigated the impact of attenuation correction on quantification when using a multiple-mouse holder for both the Inveon and microPET R4 Siemens scanners [2]. They reported quantitative differences between single- and multiple-mice mode scans when using CT-based attenuation correction and obtained less than 15% difference between the two acquisition modes in terms of measured mean ROI values extracted from [<sup>18</sup>F]FDG mice images. In 2016, Reilhac *et al* assessed the PET signal degradation when scanning two mice simultaneously scanning in the Siemens Inveon small-animal PET scanner [6]. Both simulated and experimental results showed that dual mode acquisition did not have a major impact on ROI-based analysis except in situations where uptake values in organs from the same subject were compared. However, dual-mice imaging strongly reduced the sensitivity to relative signal variations in mean and standard deviation of the measured activity concentrations in several regions of interests when mice were positioned side-by-side while no sensitivity reduction was observed when they were facing each other.

In parallel with these studies, several research teams have been specifically working on the design of dedicated holders to ensure an optimal and reproducible positioning of several animals in the field of view of the scanners. In 2009, Cheng *et al* designed a head holder for scanning two rats simultaneously in small animal PET scanners to maintain high sensitivity and to minimize repositioning error between

scans [7]. More recently, Greenwood *et al* designed a 4-mice hotel for use in a nanoScan PET/CT system (Mediso Medical Imaging Systems) [8]. They suggested that [<sup>18</sup>F]FDG radiotracer uptake in the major organs of healthy mice scanned simultaneously versus those scanned individually produced similar quantitative values, despite the expected biologic variation in radiotracer retention and excretion.

Our objective is to study which scanner could be the most appropriate to perform quantitative high-throughput mice imaging. We assessed the imaging capabilities of two PET/CT systems from the Inviscan company (Inviscan SAS). The first system is dedicated to mice and rat imaging (IRIS PET/CT) and the second is designed for non human primate (NHP) imaging (IRIS XL-260). These two systems are based on similar detector technology. The IRIS PET/CT consists in two rings of eight detectors each. The IRIS XL-260 PET/CT consists in a single ring of sixteen detectors. Phantoms and [<sup>18</sup>F]FDG tumour-bearing mice acquisitions were conducted in single and high-throughput modes with both the IRIS and the IRIS XL-260 PET/CT systems in order to evaluate the capability of high throughput between the two systems in terms of quantification.

## II. MATERIALS AND METHODS

### A. Systems Description

The PET component of the IRIS system consists in 16 modules arranged in two octagonal rings. Each module comprises a matrix of  $27 \times 26$  Cerium doped lutetium-yttrium orthosilicate crystals doped with cerium (LYSO:Ce) of  $1.6 \times 1.6 \times 12 \text{ mm}^3$ . The matrix is directly coupled to a Position Sensitive Photo-Multiplier Tube (PSPMT) (Hamamatsu Photonics). A full description of the IRIS system can be found in [9].

We also assessed the high-throughput capability on mice imaging of the new IRIS XL-260 PET, a system dedicated to NHP which has a bore size of 260 mm and a trans-axial Field-of-View of 210 mm. The IRIS XL-260 PET detector ring consists in 16 modules arranged in one single ring. Each detector module comprises a  $32 \times 32$  matrix of  $1.54 \times 1.54 \times 16 \text{ mm}^3$  LYSO:Ce crystals, coupled to a PSPMT (Hamamatsu Photonics). The IRIS XL-260 PET system has an absolute sensitivity of 2.7% for a 250-750 keV energy window measured according to the NEMA procedure [10]. Note that the IRIS XL-260 PET system's sensitivity is similar to the IRIS XL-220 PET system's as reported in [11]. The CT component consists in a micro-focus x-ray tube with a power of 80 W and a flat panel CMOS detector. The CT covers a FOV up to 210 mm in the transaxial and 85 mm in the axial directions with a single acquisition.

As the two PET systems show different detector geometry and sensitivity, we have chosen the activity levels placed in the systems' fields of view to obtain similar singles count rate values on both systems to ensure a similar behavior of the readout electronics in high-throughput mode. In addition, phantoms and mice acquisitions were performed at similar locations within the system's FOV.

### B. Phantom Studies

IQPs were used to assess the quantification capabilities of the IRIS and IRIS XL-260 PET/CT systems. These IQPs were designed to fit in the multi-mice holders as reported in [8]. They are smaller in diameter but show the same features as the IQP described in the NEMA NU-4 recommendations [10]. They are composed of a main phantom body that contains a fillable cylindrical chamber (diameter = 20 mm) and a solid part (20 mm in length) into which five fillable rods with various diameters (1, 2, 3, 4, and 5 mm) have been drilled. A lid attached to the uniform region of the phantom supports two cold-region chambers. These regions are hollow cylinders (15 mm in length and 5.5 mm in inner diameter with 1-mm wall thickness),

to be filled with non-radioactive water and air, respectively. The IQP phantoms were filled with 3.7 MBq of [<sup>18</sup>F]FDG solution each.

PET acquisitions were first performed with only one IQP placed in the central part of the FOV of both systems. Then three to six IQP phantoms were placed in the hotels described in the animal experiments section. The duration of the scans was set to 10 min each. CT acquisitions were performed right after the PET scans. We followed the NEMA NU-4 2008 standard for the analysis of the IQP data to compute the image uniformity and the recovery coefficients (RCs) for each rod. PET data were reconstructed using the iterative 3D OSEM algorithm. The calibration factor was included in the normalization file and applied during the reconstruction process. PET data were fully corrected for attenuation, random coincidences, radioactive decay and dead time. No scatter correction was applied.

### C. Animals and Xenograph Model

4T1 cells were cultured in 75 cm<sup>2</sup> culture flasks containing DMEM High Glucose (Gibco), glutamax (Gibco). Medium was supplemented with 10% foetal bovine serum (Life technologies) and 1% of Penicillin-Streptomycin (10,000 U/mL) (Gibco). Cells were grown at 37 °C in a humidified atmosphere containing 5% CO<sub>2</sub> and subcultured three times per week. The viability and number of cells were determined with the trypan blue exclusion technique.

24 female BALB/c mice ( $19.4 \pm 0.3 \text{ g}$ , 8 weeks old; Charles River) were kept at constant temperature (22°C) and humidity (40%) with 12h light/dark cycles and were allowed free access to forage and water until 4h before the beginning of each imaging procedure. Animals were housed in individually ventilated cages. A cell suspension of one million 4T1 cells in 50  $\mu\text{L}$  of PBS was injected subcutaneously into the right mammary gland under inhalation anesthesia (1.5-2% of isoflurane). All animal experiments were performed in accordance with European Institutes of Health Guidelines regarding the care and use of animals for experimental procedures and were approved by the Alsace Regional Ethics Committee for Animal Experimentation (approval identification: APAFIS#15255).

### D. Animal Experiments

One week post cells injection, the 24 mice underwent an intraperitoneal injection of [<sup>18</sup>F]FDG. The mean injected activity was  $4.28 \pm 0.19 \text{ MBq}$ . Anesthesia was induced and maintained with 1.5% isoflurane in medical air with a calibrated vaporizer for the entire procedure. Throughout the investigation, mice were kept at a constant temperature of 37°C.

The cohort of 24 mice was divided into 4 groups of 6, imaged according to different acquisition modes. Figure 1 shows a photograph of the experimental setups using the multiple-animal hotel.

1) *Animal Experiments on the IRIS system:* Six mice were used to perform high-throughput imaging acquisitions, consisting of 3 mice being imaged simultaneously as shown in Fig 1(A). A rat cell (Equipement veterinaire MINERVE, Estenay, France) was used to maintain the mice temperature and anesthesia. Mice hotels, specifically designed to fit the Minerve rat cell were used to position 3 mice per hotel. The two groups of 3 mice each underwent 60 min of dynamic 3D PET acquisitions starting 15 min after [<sup>18</sup>F]FDG injection.

The last 6 mice were imaged individually positioned at the center of the FOV. Each mouse underwent two distinct 10 min static PET acquisitions starting 15 min and 65 min after [<sup>18</sup>F]FDG injection, respectively.

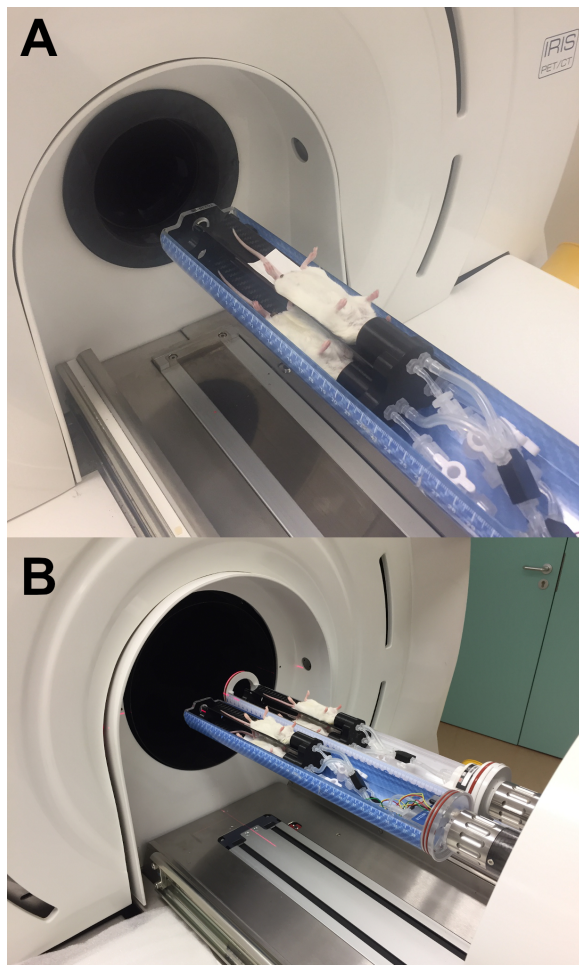


Fig. 1. Photographs of the experimental high-throughput setups using (A) IRIS PET/CT and (B) the IRIS XL-260 systems.

Data from the high-throughput and single modes were processed identically as follows. In high-throughput mode, acquired list-mode PET data were binned into 6 frames of 10 min each and reconstructed into a  $101 \times 101 \times 120$  3D volume. The voxel size was equal to  $0.855 \times 0.855 \times 0.845$  mm<sup>3</sup>. A 20s CT acquisition was performed right after each PET scan. CT data were reconstructed into a  $576 \times 576 \times 729$  3D volume, corresponding to a transaxial FOV of 80 mm, with an isotropic voxel size of 0.15 mm.

2) *Animal experiments on the IRIS XL-260 system:* Six mice were first imaged simultaneously as shown in Fig 1(B). Two rat cells were used to maintain the mice temperature and anesthesia. Two mice hotels similar to the one described above have been used to position the 6 mice into the system FOV.

The 6 mice underwent 60 min of dynamic 3D PET acquisitions starting 15 min after [<sup>18</sup>F]FDG injection. Acquired list-mode PET data were binned into 6 frames of 10 min each and reconstructed into a  $261 \times 261 \times 65$  3D volume. The resulting voxel size was equal to  $0.822 \times 0.822 \times 0.81$  mm<sup>3</sup>. A 40 s CT acquisition was performed right after the PET scan. CT data were reconstructed into a  $968 \times 968 \times 468$  3D volume, corresponding to a transaxial FOV of 210 mm, with an isotropic voxel size of 0.22 mm.

Six other mice were then imaged individually using the IRIS XL-260 system positioned at the center of the FOV. Each mouse underwent two distinct 10 min static PET acquisitions starting 15 min and 65 min after [<sup>18</sup>F]FDG injection, respectively. Data were

reconstructed into a  $113 \times 113 \times 65$  3D volume. The resulting voxel size was equal to  $0.822 \times 0.822 \times 0.81$  mm<sup>3</sup>. A 40 s CT acquisition was performed right after each PET scan. CT data were reconstructed into a  $600 \times 600 \times 729$  3D volume, corresponding to a transaxial FOV of 80 mm, with an isotropic voxel size of 0.15 mm.

3) *PET Reconstruction and Data Analysis:* For both PET systems, images were reconstructed using the manufacturer's default settings, consisting in an iterative three-dimensional (3D) ordered-subset expectation maximization OSEM algorithm (8 iterations, 8 subsets) using Monte Carlo based system matrices. The calibration factor was included in the normalization file and applied during the reconstruction process. PET data were fully corrected for attenuation, random coincidences, radioactive decay and dead time. No scatter correction was applied.

PET data analyses were performed using the AMIDE software package [12]. Ellipsoids were manually drawn on the tumors, large enough to account for the entire radiotracer uptakes. Inside the volume, a region of interest (ROI) was defined by all the voxels with a value greater than 40% of the maximum activity concentration value. The percentage of injected dose per gram value (%ID/g) was then calculated for all tumors as the average activity concentration calculated inside the ROI divided by the injected activity.

To obtain the tumor quantification ground truth, all 4T1-bearing mice were sacrificed and dissected at the end of scanning procedure. After excision, the tumors were weighed and placed in an automatic gamma counter (Hidex, Turku, Finland) for 1 min. The count obtained was converted to absolute activity using a calibration curve and then corrected for radioactive decay. The results are expressed as a percentage of injected dose per gram of tissue (%ID/g) calculated as the measured organ activity divided by its weight and the injected activity value.

We also calculated the ratios between the %ID/g values extracted from the PET images and the ex-vivo values to estimate the quantification degradation in all the studied acquisition modes. We then compared each variable between the groups using the Mann-Whitney rank test function. Statistical calculation was performed considering a  $p < 0.05$  level of significance.

### III. RESULTS

#### A. Phantom Studies

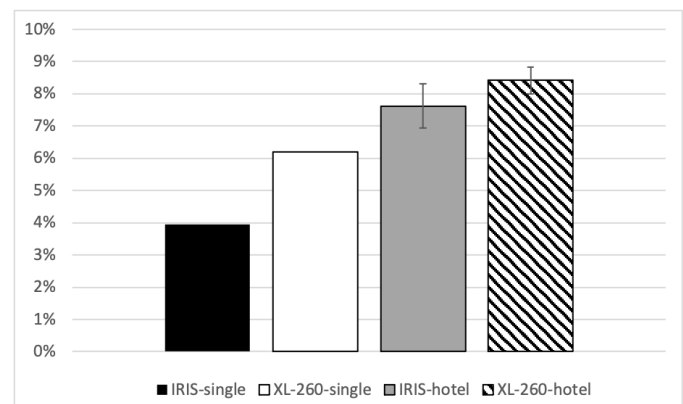


Fig. 2. Image uniformity measured for both PET systems in single- and high-throughput modes.

The image uniformity measured for both PET systems in single- and high-throughput modes are presented in Figure 2. The IRIS

system presents a slightly better image uniformity compared to the IRIS XL-260 system in high-throughput mode.

Figure 3 illustrates the experimental results reported in Table I obtained using the IQP for the two systems in both single- and high-throughput modes.

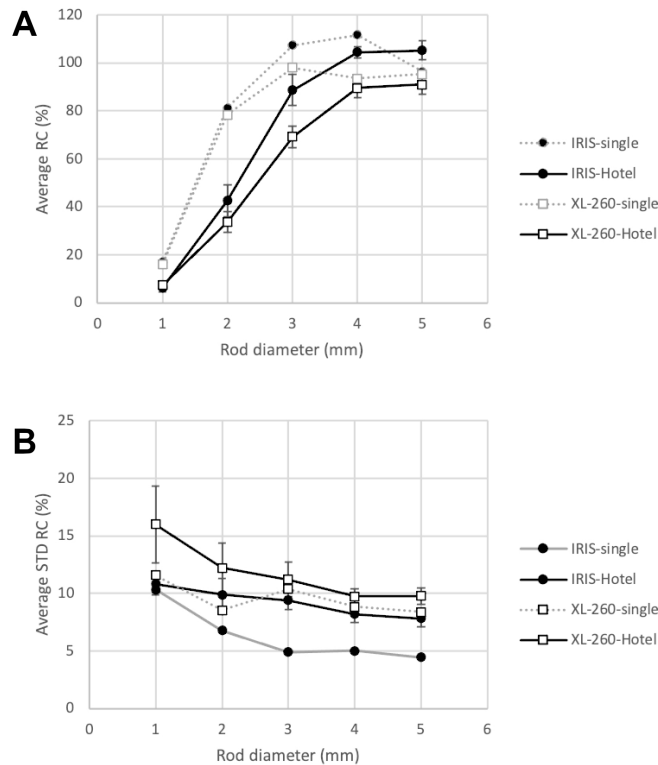


Fig. 3. (A) Recovery Coefficient values for both systems in single- and high-throughput modes and (B) the corresponding average standard deviation.

TABLE I

AVERAGE STANDARD DEVIATIONS OF THE RECOVERY COEFFICIENTS OBTAINED IN BOTH SINGLE (<sup>s</sup>) AND HIGH-THROUGHPUT (<sup>h</sup>) MODES USING THE IRIS (I) AND THE IRIS XL-260 (X).

Rod	5 mm	4 mm	3 mm	2 mm	1 mm
I <sup>s</sup>	4.5	5.0	4.9	6.8	10.3
I <sup>h</sup>	7.8 ± 0.8	8.2 ± 0.7	9.4 ± 0.9	9.9 ± 1.4	10.8 ± 1.0
X <sup>s</sup>	8.4	8.9	10.4	8.6	11.6
X <sup>h</sup>	9.8 ± 0.7	9.8 ± 0.7	11.2 ± 1.5	12.2 ± 2.1	16.0 ± 3.4

### B. Animal Experiments

Figure 4 shows the Maximum Intensity Projection (MIP) obtained in high-throughput mode using both PET/CT systems.

The use of the mouse hotel makes it necessary to present a MIP in order to demonstrate that all the tumors are clearly identified in all the animals present in the scanners' field of views in high-throughput mode.

Figure 5 shows the percentage of injected dose per gram measured in the two distinct 10 min static PET acquisitions and the ex-vivo values obtained using the gamma counter for both scanners in single mode acquisitions.

The difference in terms of percentage of injected dose per gram measured in the tumor between the two static acquisitions

follows a classic bio-kinetics behavior of [<sup>18</sup>F]FDG following an intraperitoneal injection. Furthermore, the difference in %ID/g between the last static acquisition (5 minutes before animal sacrifice) and the ex-vivo value is not statistically significant (p-value > 0.05) for both PET systems in single mode.

Figure 6 shows the percentage of injected dose per gram measured in the 60 min of dynamic 3D PET acquisitions starting 15 min after [<sup>18</sup>F]FDG injection and the ex-vivo values obtained using the gamma counter for both scanners in high-throughput mode acquisitions.

In high-throughput mode, there is a difference between the results obtained with the IRIS and the IRIS XL-260 systems. The difference in %ID/g between the last static acquisition and the ex-vivo value is not statistically significant for the IRIS system. However, there is a significant statistical difference between the last static acquisition and the ex-vivo values for the IRIS XL-260 PET system, with a p-value of 0.015.

In order to estimate the quantification degradation in all the studied configurations, we calculate the ratios between the %ID/g values extracted from the PET images and the ex-vivo values, as presented in Figure 7. Ex-vivo values were considered as the reference.

In single mode acquisitions, ratios of  $0.94 \pm 0.09$  and  $0.83 \pm 0.08$  were obtained for the IRIS and the IRIS XL-260 PET systems, respectively. In high-throughput mode, ratios of  $0.78 \pm 0.12$  and  $0.73 \pm 0.13$  were obtained for the IRIS and the IRIS XL-260 PET systems, respectively.

## IV. DISCUSSION

The concept of high-throughput imaging is an active preclinical research topic. Imaging several animals simultaneously makes it possible to meet the statistical expectations of the studies while respecting the principles of the 3Rs in the ethical framework for animal research and the care and well-being of each individual. However, it is essential to study the impact on image quality and quantitative accuracy of scanning several animals simultaneously. In PET, the increased injected dose present in the field of view, the greater attenuation or even the effects of dead time and scatter are all phenomena that can alter the quality of the image and the quantitative precision.

We have assessed the quantification capabilities of two preclinical PET/CT systems from the Inviscan Company when imaging multiple mice simultaneously. The manufacturer currently proposes 2 PET/CT systems, the IRIS PET/CT dedicated to mice and rat imaging and the IRIS XL 260 PET/CT, dedicated to large animal imaging. The two systems are based on similar detector technology but have very different detector configuration.

Most of users who have a requirement for large animal imaging as well as rodents will not be acquiring two dedicated systems, for several reasons, such as lack of space or limited budget. State-of-the-art preclinical PET/CT systems usually provide sufficient axial FOV to image the entire mouse. However for rat imaging and primate imaging this is not the case. Rat full body will most of the time be imaged in multiple scan mode. Primate imaging also requires multi scan imaging unless one organ is imaged dynamically. In the case of multi-mice imaging, a rodent dedicated system will always be preferable for practical reasons. However we evaluated whether the IRIS XL 260 PET/CT can perform multi-mice imaging with similar image quality and throughput capability.

Results show a loss in image uniformity between the single- and the high-throughput modes for both the IRIS and the IRIS XL-260 systems. The results are consistent with other similar reported studies. Greenwood *et al* reported similar degradations in terms of image uniformity and RCs values [8]. The IRIS system presents a better

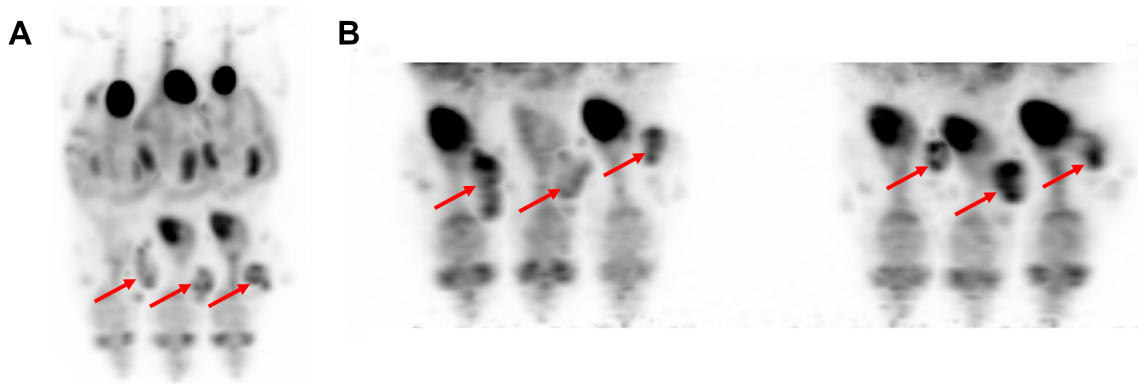


Fig. 4. (A) MIP in high-throughput mode obtained with the IRIS system (3 mice) and (B) MIP in high-throughput mode obtained with the IRIS XL260 system (6 mice). Red arrows highlight the 4T1 tumors in all imaged animals.

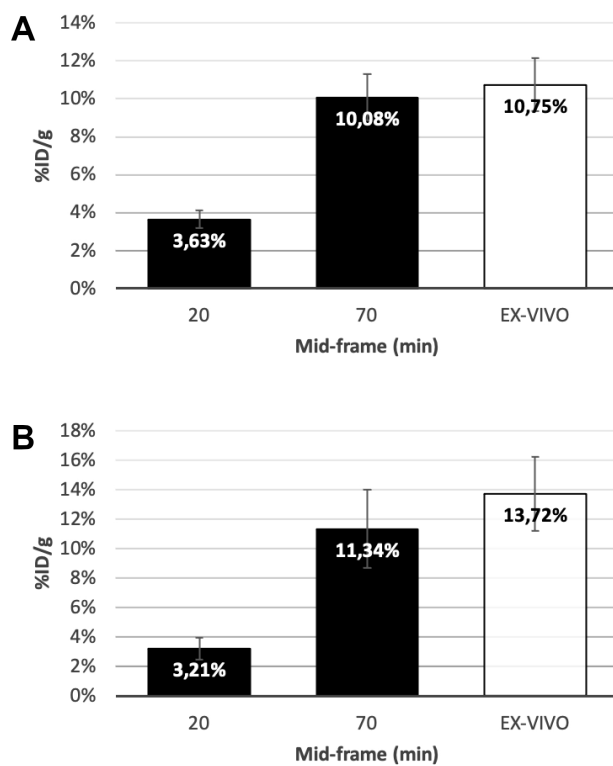


Fig. 5. Percentage of injected dose per gram measured in the two distinct 10 min static PET acquisitions starting 15 min and 65 min after  $[^{18}\text{F}]\text{FDG}$  injection and the ex-vivo values obtained using the gamma counter. The measured values obtained in single mode using the IRIS PET system are presented in (A) and (B) for the IRIS XL-260 PET system.

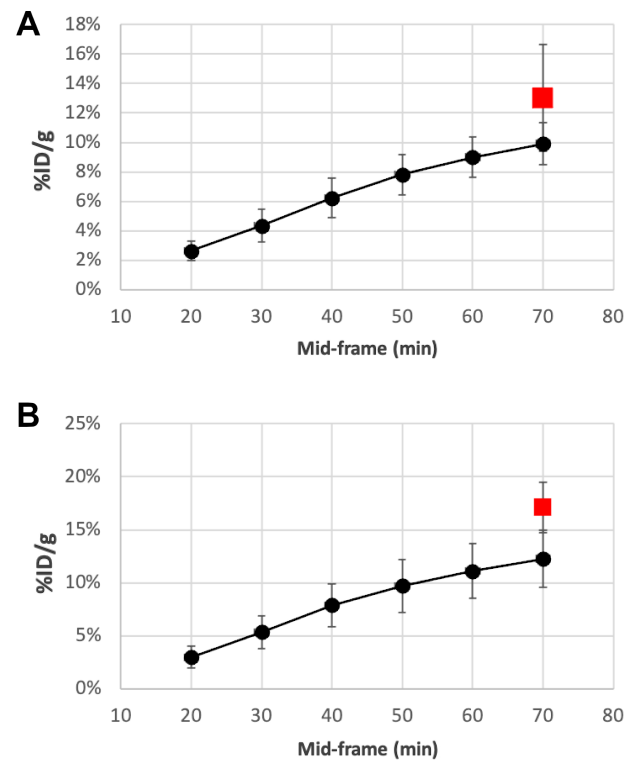


Fig. 6. Percentage of injected dose per gram measured in 60 min of dynamic 3D PET acquisitions starting 15 min after  $[^{18}\text{F}]\text{FDG}$  injection. The ex-vivo values obtained using the gamma counter are represented by the red squares. (A) and (B) represent the measured values obtained in high-throughput mode using the IRIS and the IRIS XL-260 PET systems, respectively.

image uniformity compared to the IRIS XL-260 system in high-throughput mode, although the loss in uniformity is stronger in IRIS compared to XL-260.

In terms of Recovery coefficients obtained in high-throughput mode, using the single mode as reference, results show recovery coefficients losses (from 0.17 to 0.06 and from 0.16 to 0.02 for the IRIS and the XL-260, respectively) for the smallest rod of the phantom, which go along with the highest standard deviation of the RCs. RC numbers were slightly lower for the IRIS XL-260 than RCs obtained with the IRIS system. Similar losses in RCs were reported in [5] where RC for the 2mm rod went from 0.7 to 0.47 and the RC for the 1mm rod went from 0.35 to not visible. In [8], the authors

also reported comparable losses in RCs (RC for 1 mm dropping from 0.25 to 0.06).

Several parameters may explain these results. First of all, the scatter fraction for the IRIS is slightly higher than the one for the XL-260 system. Also, while the mean values in the IQP uniform region are similar for both systems, extracted values corresponding to the rods are lower for the XL-260, despite similar spatial resolutions values. This could be explained by the difference between the two system matrices used to reconstruct the data, but also the convergence of the reconstruction algorithms which could be different as we used the manufacturer's default settings. We also observed an over-estimation of the RCs ( $\text{RC} > 100\%$ ) using the IRIS system for the larger rods.



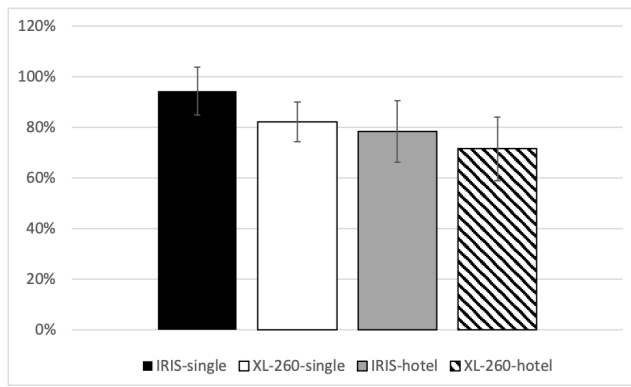


Fig. 7. Ratios between the %ID/g values extracted from the PET images and the ex-vivo values using both PET systems in both single- and high-throughput modes.

Similar over-estimation of RCs were also reported in [5]. Kim *et al* recently reported similar results demonstrating the impact of the reconstruction algorithms and parameters but also the use of the maximum value in the rods during the data processing, which can lead to an over-estimation of the RCs compared to the average or peak values, which could limit this phenomenon [13].

Overall, the results seem to indicate that the IRIS system offers a better performance in terms of image uniformity and RCs in both single- and high- throughput mode acquisitions when imaging several mice.

The quantitative assessment was also conducted in single and high-throughput modes on [<sup>18</sup>F]FDG tumor-bearing mice. Several studies reported reduced quantification accuracies up to 15% when scanning multiple animals simultaneously compared to conventional single animal scanning [2], [5] - [7]. We obtained similar results with both the IRIS and the IRIS XL-260 systems. Aide *et al* reported a 90% mean ratio between PET quantitative data and ex-vivo counting [5], while we obtained similar ratios in single mode acquisition ( $0.94 \pm 0.09$  and  $0.83 \pm 0.08$  for the IRIS and the IRIS XL-260 systems, respectively) and slightly lower ones in high-throughput acquisition mode. The IRIS system presents good performance in terms of quantification, despite the absence of scatter correction, which partly explains the loss in RC and uniformity observed in high-throughput mode. Although it presents a large transverse field of view allowing to image a greater number of animals simultaneously, the loss in RC and uniformity is slightly more important in the case of the IRIS XL-260 system.

Although these two scanners are based on the same detection technology, their geometries give them significantly different performance. The axial coverage and the diameter of the detection ring differ drastically between the two scanners. This leads to significantly lower sensitivity in the case of the NHP scanner (2.7% absolute sensitivity compared to 8% for the IRIS considering an energy window of 250-750 keV, [9]). In addition, the axial coverage of the IRIS system makes it possible to image the entire body of a mouse, unlike the IRIS XL-260 system for which a significant proportion of the activity is found outside the field of view. Despite a shorter axial field of view, the IRIS XL-260 offers the possibility of simultaneously imaging a large number of animals thanks to its wide transverse field of view. In addition, it presents sufficient quantitative performance for studies focusing on a specific organ. The disadvantage of imaging a large number of animals ( $n \geq 6$ ) remains to lower the amount of activity injected per animal to ensure a low level of count loss due to detector dead-time. Furthermore, the IRIS XL-260 presents itself as a good alternative in the case of studies using an expensive radiotracer

and/or with a short half-life, thus making it possible to ensure that all the animals will be injected with the same specific activity. Finally, this study was based on results extracted from acquisitions performed 15 minutes post-injection. Investigating the quantitative capacities of these systems in the context of compartmental analysis studies of the kinetics of a radiotracer would require a completely different methodological approach, such as the use of catheters and injection pumps. However, Cheng *et al* have demonstrated that the challenge relating to such studies remains essentially technical because their results showed that the difference in Ki caused by dual scanning as opposed to single scanning was not statistically significant [7].

## V. CONCLUSION

Our objective was to study two commercially available PET/CT systems with different detector ring geometric arrangement and establish if one system in particular is more appropriate to perform quantitative high-throughput mice imaging. The IRIS PET/CT system is dedicated to mice and rat imaging, the IRIS XL 260 is dedicated to NHP imaging. Phantoms and in-vivo studies have made it possible to highlight their capacities to perform high-throughput acquisitions.

The results suggest that the IRIS system configuration provides more accurate quantitative results when aiming for whole-body high-throughput imaging. The large transverse field of view of the IRIS XL-260 makes it possible to image a greater number of mice simultaneously, which may be useful in specific cases such as studies using an expensive radiotracer and/or with a short half-life. However, it maybe preferable to reduce the number of animals in order to minimize the quantification bias by considering a full axial coverage of the animals while maximizing the sensitivity.

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