MOLECUBES
MODULAR
BENCHTOP
IMAGING

INCREASED PET THROUGHPUT: the mouse hotel

In preclinical molecular imaging throughput matters. If large cohorts of mice need to be scanned, a workflow allowing for reproducible speed optimization in view of quantification is often a must [1]. The best strategy to increase imaging throughput is to image multiple animals within a single scan, reducing user-variability - while managing tracer volumes. This is particularly helpful when radioactive isotopes with short half-lives are used (e.g. 11C and 68Ga for PET-studies), when the radiochemical yield or specific activity of new compounds is low or when complex dynamic studies with long acquisition times are set up. In all these cases the more animals that can be evaluated with one radiosynthesis batch, the better. Furthermore, the total imaging time can be reduced significantly so is the total operating cost related to the study. MOLECUBES has designed its systems to facilitate this throughput in 2 ways: an animal hotel bed in combination with highly sensitive modular systems.

The MOUSE hotel

MOLECUBES developed a mouse hotel bed, Figure 1, that can hold up to **four mice (up to 35g/mouse) with fully integrated anaesthesia delivery and scavenging, respiratory monitoring and controlled animal heating** on all positions. In addition, this bed provides temperature monitoring on one position and is compatible with both our β-cube PET system and X-cube CT system.

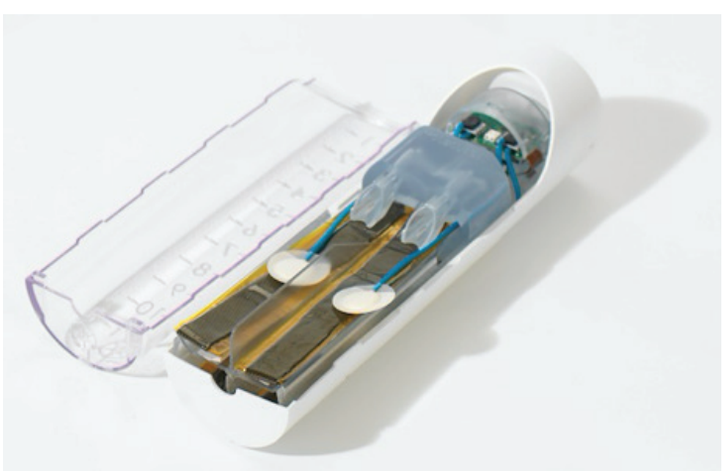
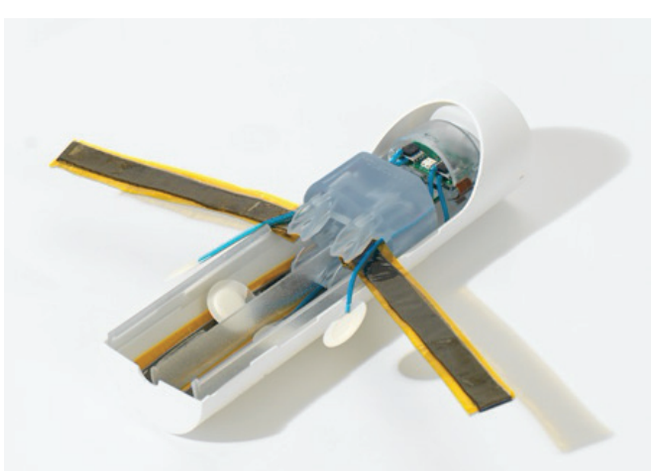


Figure 1:mouse hotel with matching cover.



hotel options showing the 2-layer construction

integrated heating and breathing monitoring.

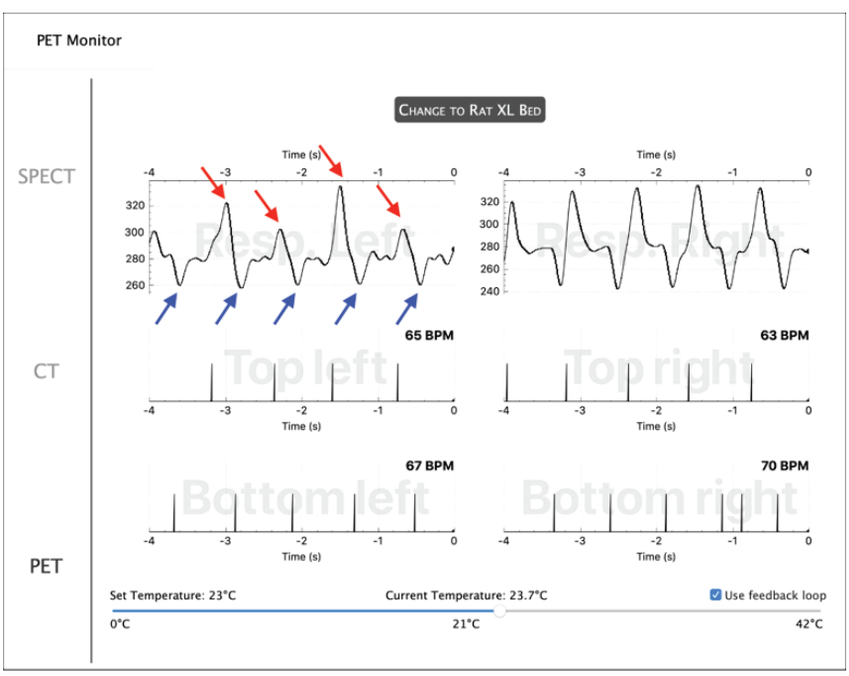
matching docking station for animal preparation

The mouse hotel bed allows the user **to scan either one, two, three or four mice simultaneously using 1.5% isoflurane anaesthesia and an oxygen flow of 600-800 ml/min.** Plugs are included to prevent anaesthesia leaking from unused positions when scanning less than four animals. **The mouse hotel can contain mice having a weight up to 35g/mouse, however, it is possible for larger animals to fit the bed depending on body structure and/or tumour volume.** The respiration of each animal can be monitored by placing a pressure pad underneath the chest of each animal. The respiration signal as well as the number of breaths per minute are visualised in the graphical user interface, and also the breaths per minute are shown.

The animals body temperature is maintained using carbon heating pads which are controlled via the GUI by either setting the power of the pads to a certain percentage in order to maintain a stable temperature or – when using the rectal probe on one of the animals – by setting the temperature to a certain value which is maintained via the feedback loop. In the latter case, the current measured temperature is indicated in the GUI as well. Respiratory or cardiac gated imaging and cardiac monitoring is not possible with the mouse hotel.

Technical Specifications

Dimensions	27.5 cm length, 7.2 cm diameter
Weight/animal weight	35g/mouse, maximum of 4 mice
Anaesthesia	1.5% isoflurane mixed with oxygen at a flow of 600-800 ml/min
Heating	Carbon pads, temperature < 42 °C
Respiratory monitoring	Yes



As illustrated in Figure 2, the graphical user interface allows real-time monitoring of both the respiratory signal as well as the breathing rate for each animal. Furthermore, the body temperature of each mouse can be maintained via the heat pad with the option of a feedback loop using the rectal probe.

Figure 2. Mouse hotel respiration signal. Red arrows indicate respiration peaks of the animal positioned top left, blue arrows indicate respiration peaks of the animal positioned bottom left. Below the combined respiration signal, the individual breaths per min can be seen.

High sensitivity, modular design

Thanks to the high sensitivity of our PET system and uniform resolution of the entire field of view, our β-cube is an ideal system **to evaluate multiple animals simultaneously in a quantitative way [2]. Peak sensitivity of the system is at 12,6% and sub-millimeter image resolution is guaranteed.**

With multiple animals in the field of view it is important that image quality, resolution and quantitative accuracy are maintained throughout the entire field of view. Thanks to the depth of interaction methodology, our β-cube PET system has a uniform submillimetre resolution (Figure 3) over the complete transaxial and axial field of view. In addition, quantitative accuracy and uniformity can be demonstrated throughout the entire imaging volume (2% and 4% deviation respectively).

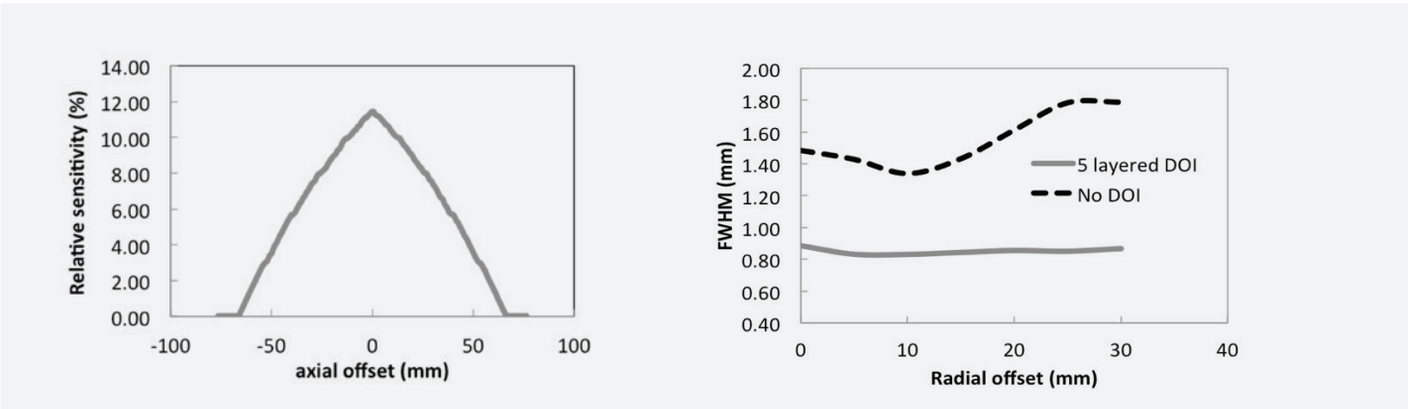


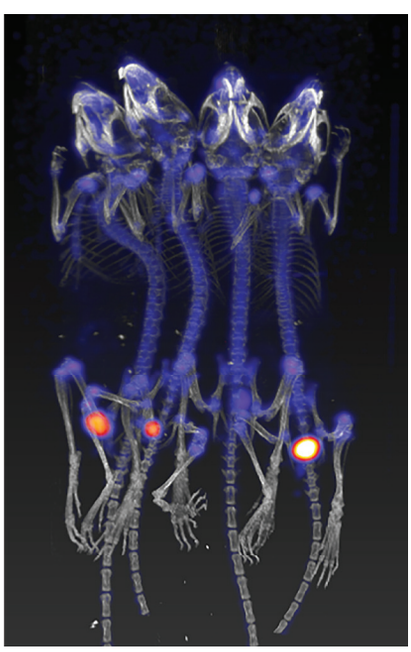
Figure 3 Left: Peak sensitivity (NEMA) over the field of view.
Right: image resolution over the field, with the effect of Depth of Interaction modelling showed.

Given their small footprint and modular design, multiple ß-cubes can easily be installed side by side and interconnected to further increase the animal throughput. Figure 4 shows a PET/PET/CT set-up allowing the researchers to scan up to 8 mice simultaneously.

Multiple biotech and pharma clients have already selected MOLECUBES because of these options, as their main imaging platform in large compound or drug screening studies

Application

To demonstrate the functionality of the mouse hotel a static PET/CT scan was performed. Four mice were injected with 2.2 MBq [18F]-NaF each, 30 minutes prior to a 10 min, one bed position PET scan. Following the PET scan, a 1.5 minute general purpose CT scan was acquired. The PET image was reconstructed using 30 iterations of the 3D OSEM algorithm and a voxel size of 400um. The CT image was reconstructed at 200 um voxel size using an iterative reconstruction algorithm. In Figure 5 the coregistered CT and PET image can be appreciated.



References

1. Aide N, et al. Eur J Nucl Med Mol Imaging. 2012; 39:1497–1509
2. Krishnamoorthy S, et al. Phys Med Biol. 2018; 63(15):155013

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