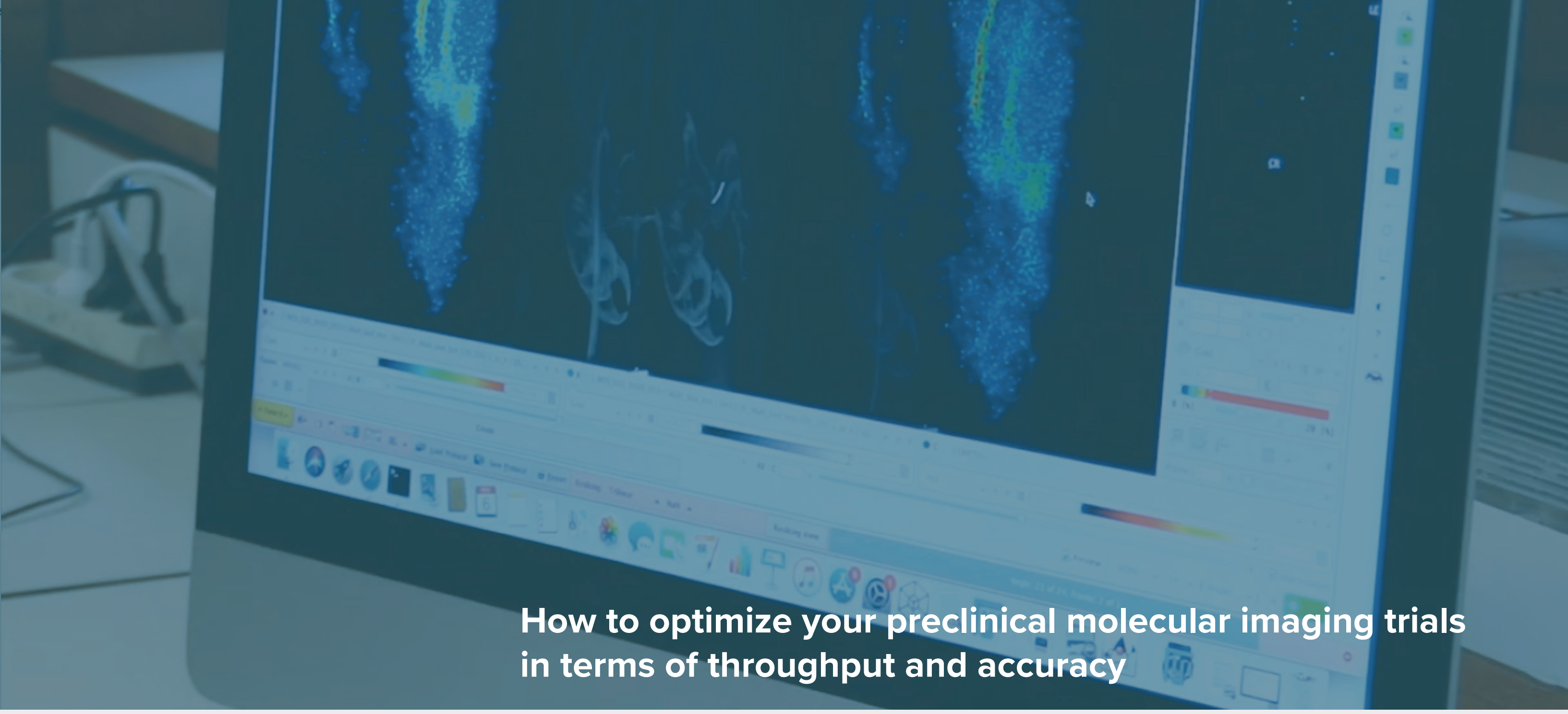


How to optimize your preclinical molecular imaging trials in terms of throughput and accuracy

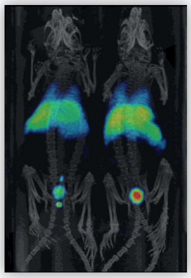
MOLECUBES
MODULAR
BENCHTOP
IMAGING

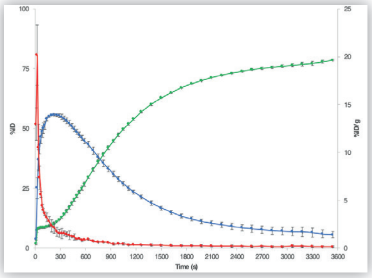
How do I facilitate error-free, effective imaging trials on small animals? This is one of the key questions we identify within university research groups, the pharmaceutical/biotech sector and CRO companies. Besides scanning time, critical bottlenecks typically include animal preparation, image post-processing and quantification. In this white paper, we wish to share our point of view on the most crucial elements in the imaging chain as well as provide you solutions to increase the throughput and accuracy of your trials.

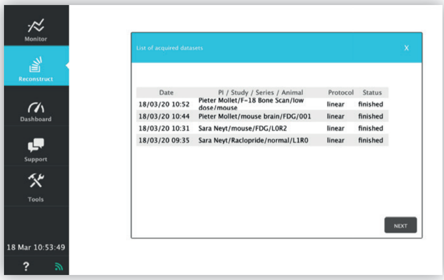
1. Ensure integration from animal preparation through to image post-processing

Imaging is about a lot more then the right scanner for the job. Integration of the entire imaging work- and dataflow improves speed of the end-to-end chain of activities and quantification accuracy. Firstly, **integrated animal preparation and monitoring - preferably in vicinity of the scanner** – before and during the scan not only improves animal welfare but also the reproducibility of results. This applies especially in longitudinal studies where controlled physiological monitoring is crucial. Secondly, an **intuitive user interface with automated co-registration** coupled to pre-set scan protocols reduces scan set-up time. Finally, a **universal data format ensuring compatibility with post-processing and data management tools** is a catalyst for accurate reporting, allowing direct uploading for visualisation and quantification (e.g. VivoQuant, PMOD) and study planning and follow-up (e.g. iPACS, cloud storage).

Central data management for study planning, data storage (images and quantification) and statistical analysis (e.g. iPACS)







Step 1
Animal preparation and monitoring prior to the scan

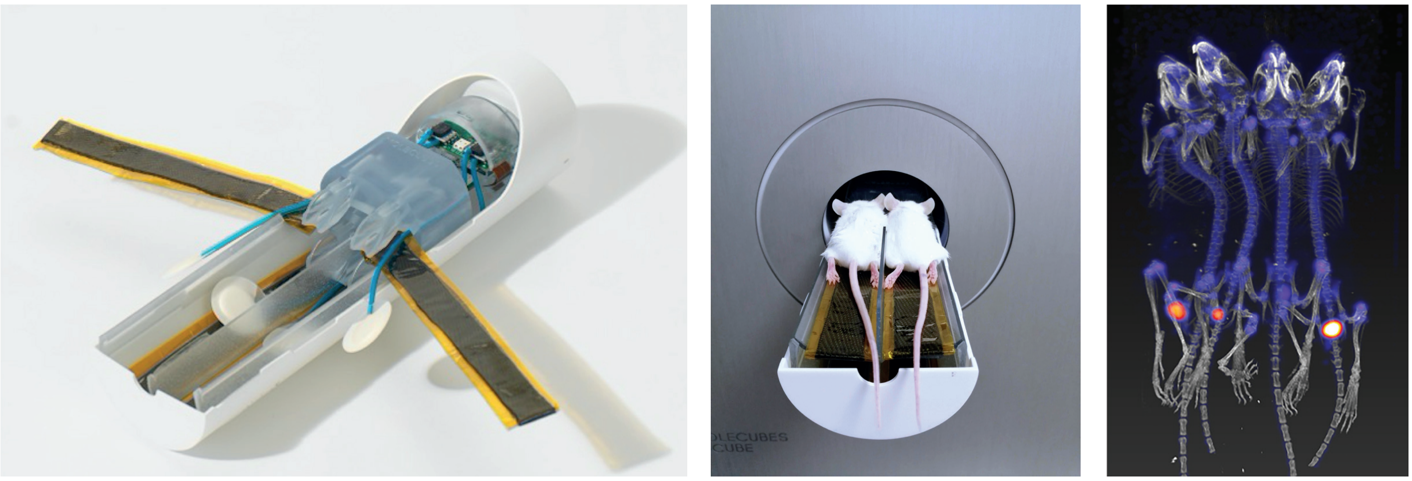
Step 2
Visualization of DICOM data

Step 3
Quantitative output with low error margin

Step 4
Storage on server or cloud compliant with organization policy

2. Ambition a high throughput scanner set-up

Recent improvements in our molecular imaging technology can speed up the scanning workflow as follows. Firstly, adverse to mainstream approaches, a choice for modular systems inherently facilitates **synchronous scanning**. By separating the modalities in different units, one modality does not block the other while scanning. When on top of that, a multi-animal bed stage can be deployed the number of scanned animals within a fixed timeframe is further optimized. Secondly, **high sensitivity** systems reduce scan time significantly even at low injected doses. This benefit also allows a higher number of animals to be studied with one radiosynthesis batch. Finally and cruicially, the separation of acquisition and reconstruction servers ensures the **parallel acquisition of data and reconstructions** of previous scans with one process not impeding the other.



Example of multi-animal bedstage (four mice) with imaging result with PET/CT scanner system

3. Facilitate scalability, ensure uptime

Scalability is essential for accommodating future capacity or modality needs. Firstly, **plug-and-play capacity upgrades** of a specific modality is needed to scale up the number of scanned animals without excessive space adaptation cost or equipment investments. Secondly, **compatibility with other modalities** is an important driver for both future expansion of imaging capabilities and integration with current hardware and software.

Finally, as scanner fall-out can heavily impact study continuity, ensuring **high uptime** is crucial in the decision-making process. Besides the inherent stability of the scanners, system modularity reduces the negative impact from scanner failure as one modality can operate fully independently from the other.

Example of modular, lab compatible imaging set-up

Example comparison of MOLECUBES β-CUBE/X-CUBE combination vs. integrated PET/CT systems

1. Ensure seamless integration from animal preparation to image post-processing	**β-cube / X-cube combination** *(high sensitivity/resolution PET/CT)*	**Integrated PET/CT systems**
a. Integrated preparation and monitoring, preferably in the vicinity of the scanner	MOLECUBES' docking station with built-in monitoring can be positioned adjacent to other scanners meaning efficient multi-animal preparation and integrated physiological monitoring is possible before and during the scan.	In standard integrated PET systems, the animal is prepared typically on the system itself, hampering the possibility to perform integrated physiological monitoring of the animal before and during the scan.
b. Intuitive user interface with automated co-registration	MOLECUBES' intuitive user interface allows the user to go from acquisition to reconstruction in less than 10 clicks. The interface can be operated from a tablet or work station adjacent to the CUBE. Preset options on PET and CT protocols are easily added.	Software of integrated systems typically require extensive training and a high number of manual actions before launching and reconstructing a scan is possible. This results in a higher risk for human error and a slower workflow.
c. Compatibility with post-processing and data management tools	MOLECUBES' DICOM format and automated coregistration are compatible with all software postprocessing packages available on the market (e.g. cloud storage, key data management and post-processing tools).	For integrated systems, the main focus is on in house software rather than on compatibility with external providers, causing limited user freedom.
2. Go for a high throughput scanning set-up		
a. Synchronous scanning	A modular PET/CT set-up allows parallel scanning in multiple modalities with room for up to four mice per scanner in a mouse hotel with monitoring.	Although multi-animal bedstages exists, using one modality blocks the other modalities for use in an integrated system
b. High sensitivity	The β-CUBE (PET) reaches peak sensitivity of 12.4% which by NEMA standards, is currently the highest on the market. Also, the X-cube (CT) allows low dose imaging, avoiding animal radiation therapy.	Best-in-class integrated systems (with NEMA resolution below 1.2 mm) achieve only a maximum of 9% peak sensitivity according to NEMA standards
c. Parallel acquisition and reconstruction	MOLECUBES' scanners have separate acquisition and reconstruction servers to allow for parallel acquisition and reconstruction of scans.	Typically, integrated systems will house both acquisition and reconstruction in one unit, thus requiring the sequential acquisition and reconstruction of data resulting in the slowing down of workflows.
3. Facilitate scalability		
a. Plug-and-play capacity upgrade	All CUBES are available by modality, upgraded with extra modalities without downtime and measure 54x54x54 cm^3, fitting three CUBES on a 2 meter lab table. No CUBE weighs over 105 kg.	Best-in-class integrated PET systems' size is 220x150x90 cm^3 minimally, often requiring space adaptations and purchase of full-fledged system at high cost, even for small capacity upgrades
b. Compatibility with other modalities	MOLECUBES CT, PET and SPECT systems are fully compatible with other modalities (e.g. with MRI, optical systems).	Integrated systems typically offer limited compatibility with other system vendors.
c. High uptime	Even in the case a CUBE is failing, non-failing modalities remain operational at all times due to the full independence of each module.	In case of system failure, integrated modalities are non-operational, with higher potential impact on study continuity vs. modular systems.