PRECLINICAL IMAGING

PET Imaging: Past, Present, and Future

A review of PET imaging technology and its potential in preclinical research

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Innovation with Integrity

Introduction

As a highly specific functional imaging technique, positron emission tomography (PET) imaging has found broad application in clinical diagnostics. Following the first clinical PET scanners, smaller more compact systems for small animal imaging were introduced in the mid-1990s and quickly became a popular tool for preclinical research. PET uses small amounts of radioactive tracers to image important cellular and molecular processes in living subjects, with applications in oncology, cardiology, neuroscience, immunology, theranostics and basic life science research. These radioactive tracers have different rates of uptake depending on the type and function of tissue involved, which can be visualized and quantified.

The ability of PET to monitor biochemical processes and detect the expression of some proteins allows researchers to obtain a series of snapshots into a subject's pathophysiology, visualizing molecular-level information before any anatomic changes are detectable. This molecular insight provides clinicians with a means to characterize disease progression and therefore start treatment earlier, and enables researchers to develop therapeutics that target early stages of disease.

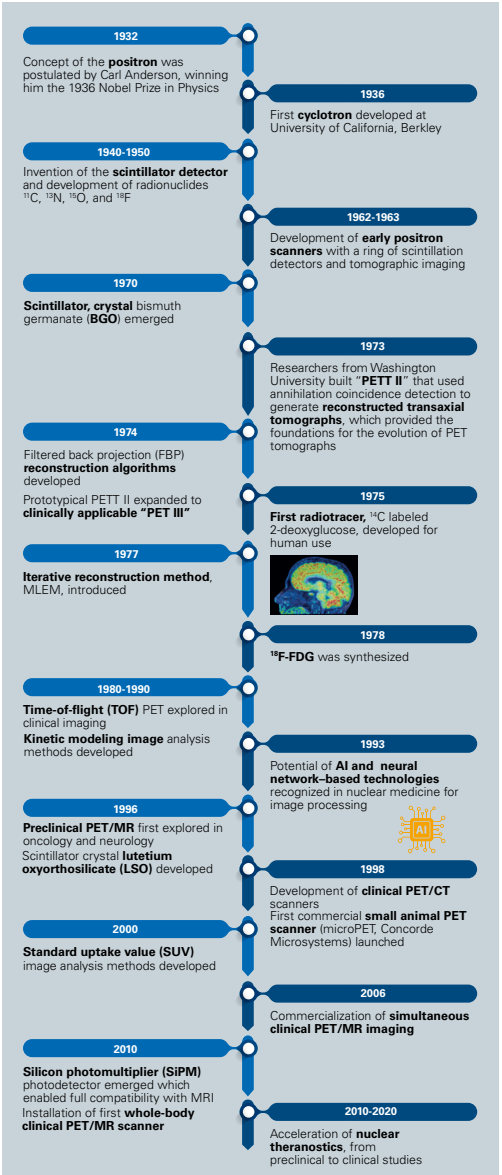
This paper reviews the journey of preclinical PET imaging, from its inception in the late-20th century to the most advanced multi-modal configurations and their application in clinical and pharmaceutical research. We discuss the work being done by PET experts at Bruker to address some of the remaining challenges facing PET imaging. We also review the potential developments that could advance the PET imaging field in the coming years.

The early days

To appreciate the impressive capabilities of modern PET technology it is important to understand how early developments have led to its widespread use, first in clinical diagnostics and later in preclinical imaging. The discovery of the positron in the 1920s, the use of radionuclides in biomedical studies, and the subsequent invention of the cyclotron in the 1940s led to the creation of a positron detection tomograph that incorporated the fundamental features of our current PET systems [1]. Since then, parallel advances in instrument design, acquisition electronics, radiochemistry, and data processing have continually improved PET sensitivity.

A notable advancement that set the stage for PET was the development of a cyclotron in the 1950s that could produce short-lived, positron emitting radionuclides. At the time, the biomedical application of short-lived radionuclides had been called into question given their limited half-lives, but researchers at Washington University and, later at Massachusetts General Hospital (MGH), advocated for their optimum decay characteristics and chemical properties for medical research. This, in turn, led to the development of the smaller and more practical negative-ion cyclotron, in which the particle beam can be split into several beam lines, making it possible to irradiate several targets simultaneously [2]. Not only were these cyclotrons self-shielding with lower energy requirements than their positive-ion counterparts, but their reduced installation and operating costs made PET technology more accessible to a greater number of researchers.

As cyclotron evolution continued throughout the 1960s and 70s, it catalyzed great leaps in PET radiochemistry. The first radiotracer developed for use in humans was 2-deoxyglucose (DG) for the measurement of brain activity, which was initially radiolabeled with ^{14}C and extensively used by Louis Sokoloff and colleagues to study energy metabolism in the brain [3] [4]. Based on Sokoloff's pioneering work in the field of PET functional imaging and neuroscience, ^{18}F-fluorodeoxyglucose (^{18}F-FDG) was synthesized in 1978 by Ido et al [5]. The use of fluorinated deoxyglucose was a huge step in the history of PET and ^{18}F-FDG has since become the most widely used radiotracer. Its success is attributed to the properties of deoxyglucose that allow uptake and trapping in metabolic active cells, such as in tumors, the brain, heart muscle, and areas of inflammation. In addition, its optimal half-life of about 110 minutes makes it easier to transport from production sites to hospitals.



These advances in radiochemistry, and their subsequent impact on clinical neurology and oncology, have been a major driver for the developments in PET scanner technology [6].

The 1990s saw a flurry of activity in nuclear molecular imaging (NMI). PET instrument design continued to advance, with the development of detectors and scintillators that could push the limits of resolution closer to the fundamental limits imposed by physical processes associated with the decay of the radio tracers. PET scintillators absorb gammas and produce a flash of photons that is sensed by the photodetector and converted into an electrical signal. The performance of positron cameras is therefore linked to the properties of the scintillator crystals. Bismuth germanate (BGO) emerged in the early 1970s and quickly became the most popular scintillator crystal for PET scanners, due to its gamma-ray detection efficiency and ability to improve PET scanner sensitivity. This improved sensitivity made it possible to shorten scan times and/or maintain low tracer activity [7].

Later, a new scintillator crystal, lutetium oxyorthosilicate (LSO), was discovered to have a higher and faster light output than BGO for PET imaging [8]. This leads to an improvement of spatial, energy and time resolution of PET systems. Their respective impact on the image quality is a more precise localization of the impinging gammas, better rejection of scattered gammas and less chance to register random coincidence events. The combined resulting effect is a sharper image with less noise [6].

During this time of accelerated PET innovation, instruments that combined additional modalities began to emerge. Although PET provides valuable physiological information, there was a clear need for complementary anatomical information to gain a more complete picture of disease and treatment outcomes. Instruments that combined PET and computed tomography (CT) images were the first to emerge in the clinical setting and their potential, particularly in the field of oncology, drove its adoption. Unifying the metabolic data from PET with anatomical information from CT offers more accurate tumor staging and assessment of treatment responses and has proven itself over the last two decades as a cost-effective clinical tool, with the first systems entering medical centers in the early 2000s.

This first introduction of PET/CT into hospitals coincided with the development of small animal PET scanners for preclinical research. The ability to use the same radiotracers in humans and animals and the identical technology used between human and small animal PET instruments make it a highly translatable tool into the clinic. Having a non-invasive imaging tool that allows researchers to longitudinally observe disease progression in small animals or their response to therapies is highly valuable in biomedical research, and the ongoing improvements in spatial resolution have enabled scientists to break new ground in fields such as oncology, neurology, and cardiology.

Instrument manufacturers applied the innovations in clinical PET scanners to the design of small animal scanners, and the first commercial platform – Concorde Microsystem's microPET series – was launched in the late 1990s [9]. This innovation transfer extended to the application of PET/CT to preclinical imaging, but researchers in this field took multi-modal PET one step further and developed instruments that incorporated magnetic resonance imaging (MRI). These small animal PET/MR scanners provided superior soft tissue contrast compared with PET/CT and have driven cutting-edge innovations over the last three decades.

Dr. Peter Bruyndonckx, system architect nuclear molecular imaging at Bruker, comments on PET/MR enabled by Bruker's MRI technology:

"In the 1990s, PET/MR was a problem because of the technology available. It was impossible to include all of the PET hardware within the MRI scanner without them having any impact on each other. So, PET/CT was the image technique of choice. Now as the technology has advanced, the ability to simultaneously perform PET and MRI has proven to be an important tool in pre-clinical and clinical applications."

Preclinical imaging: where are we now?

Until relatively recently, cost was a limiting factor for the uptake of PET in preclinical research. Now, there are many features of modern PET systems that address this barrier, such as increasing the number of small animals that can be imaged simultaneously with advanced animal cradles; improved quality of LSO detectors, driven by clinical demand; and increased number of cyclotrons capable of producing radioactive tracers. In addition, more hospitals and medical centers are now able to produce radiotracers themselves and often provide surplus to researchers at a lower price.

The ongoing effort to improve detectors has led to the development of PET scanners with higher sensitivity and better ability to exclude random events that degrade image quality. As hardware has improved over the years, the focus of PET innovation has shifted to optimizing PET data with better image reconstruction and analysis methods.

Image reconstruction

Image reconstruction is a fundamental part of PET imaging, generating 3D tomographic images of the tracer's spatial distribution based on the position and timing of the detected annihilation gammas. In the early days, image quality was limited by artefacts and scatter correction methods were limited. But demand for increased image quality in clinical PET drove advances in preclinical PET, and the technology benefitted from the advances that were occurring in parallel in other imaging technologies such as SPECT and Compton cameras.

Analytical PET imaging reconstruction methods, such as filtered back projection (FBP), were the first image reconstruction algorithms to be introduced for preclinical PET imaging and remain reliable tools for researchers with or without extensive mathematical expertise. The low computing power requirements of FBP were ideally suited to the less advanced computer technologies available at the time but as a relatively simple analytical model, it faces some limitations such as the production of artefacts and noise in the images (outlined in Table 1).

An alternative approach – iterative reconstruction – was developed to overcome these barriers. The main iterative method, maximum likelihood expectation maximization (MLEM), improves image quality because, unlike FBP, it models the statistical nature of the positron emission process. It can also include the contribution of each degradation effect in the probability of detection, so no pre-corrections of the data are required. However, there are some tradeoffs that come with these advantages, such as the need for high computational power that requires efficient graphics processing units (GPUs) to achieve reasonable reconstruction speeds, and greater noise that results from more iterations (higher resolution) (**Table 1**).

	Advantages	Disadvantages
Analytical (FBP)	✓ Relatively easy to implement numerically (Fourier transforms) ✓ Not computationally demanding ✓ Can be made very fast ✓ Algorithm is linear ✓ Used by the NEMA NU 4-2008 protocol* for comparing preclinical PET scanners.	✗ Introduces artefacts in the image due to gaps in sinograms ✗ Analytical models are too simple to account for activity not contained in the LoR ✗ Degradation effects (randoms, scatter, attenuation) are not included in the model. User must pre-correct the data before applying the algorithm, introducing noise ✗ Does not account for the statistical nature of the positron emission process, introducing noise.
Iterative (MLEM, OSEM, MAP)	✓ Analytical model accounts for the statistical nature of the positron emission process ✓ Takes into account degradation effects, so no pre-correction is required ✓ Gaps in sinograms are taken into account ✓ Good statistical properties, as unbiased estimators and are convergent.	✗ Computationally demanding, expensive ✗ Reconstruction time is relatively slow ✗ Non-linear method ✗ Hard to determine the optimal number of iterations, depends on the statistical quality of the sample ✗ Tradeoff between resolution and noise.

Table 1: Advantages and disadvantages of analytical and iterative algorithms for PET image reconstruction. LoR = line of response; FBP = filtered back projection; MLEM = maximum likelihood expectation maximization; OSEM = ordered subset expectation maximization; MAP = maximum a Poseriori. *National Electrical Manufacturers Association (NEMA) standard NU 4-2008 [10].

Additional iterative methods have been developed to overcome these challenges. For example, ordered subset expectation maximization (OSEM) together with more advanced GPUs have been designed to speed up traditional MLEM algorithms. Although initially slow, Maximum a Posteriori (MAP) techniques were developed to reduce noise and have since improved in speed (**Figure 1**).

Dr. Josep Oliver, senior NMI image reconstruction expert at Bruker, works on improving the reconstruction algorithms for PET users to maximally exploit the capabilities of the hardware. He comments on the recent advances in PET image reconstruction enabled by Bruker's technology:

"To reduce noise levels in MLEM reconstructed images you can use MAP, based on Bayes' theorem, which allows us to introduce the penalty function. The intensity of the noise reduction is modulated by the hyper parameter, known as β. The higher the β parameter, the stronger the noise reduction, but this comes with a resolution trade-off. Bruker offers two pre-settings for MAP, 'recommended β' and 'high-β', which allow users to find the right balance for them between noise reduction and resolution."

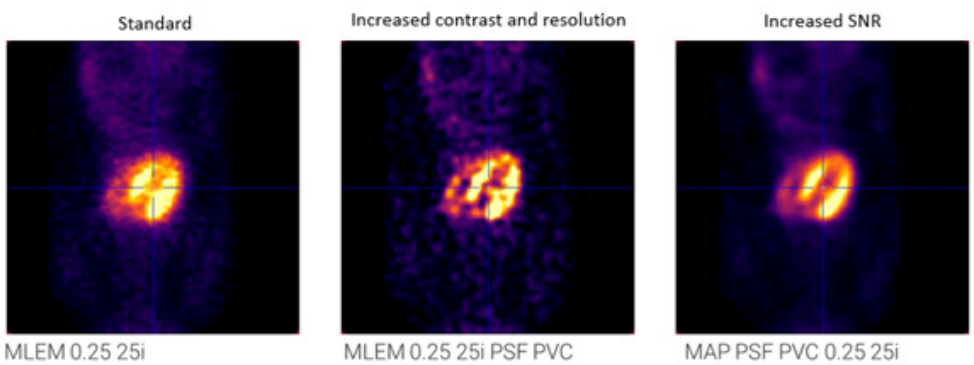


Figure 1: Positron emission tomography (PET) images of mouse hearts, showing the implementation of Maximum a Posteriori (MAP) to reduce noise. Left column shows standard maximum likelihood expectation maximization (MLEM) reconstruction without MAP, the middle column shows with the recommended beta parameter settings, and the right column shows the maximum beta parameter.

Image analysis

Once PET data acquisition is completed and after reconstruction of the corresponding images, analysis methods are needed to extract the functional and quantitative information associated with the images. Two primary PET image analysis methods – 'simple' standard uptake value (SUV)-based analysis and 'detailed' kinetic modeling – have been developed to achieve this.

Kinetic modeling was initiated with the use of gaseous tracers ^{15}O-O_2 /-CO_2/-CO in early human PET in the 1980s. Now, as a fully quantitative method, it allows both clinicians and researchers to track the kinetics of a tracer and, using a mathematical model, convert the tracer concentration and its distribution in tissue into physiological information. In preclinical imaging, achieving stable animal physiology – temperature, respiration, and heartrate – is vital for accurate kinetic modeling, and is one of the requirements of preclinical PET systems for researchers implementing this method.

SUV-based methods were developed in the early 2000s to standardize PET quantification for measuring response to human oncology treatment – a requirement recognized by the European Organization for Research and Treatment of Cancer (EORTC) [11]. SUV is one of the most widely used image analysis methods for ^{18}F-FDG PET studies and is a simplified measure that represents the ^{18}F-FDG uptake within a tumor, measured over a certain interval after administration.

Dr. Geoffrey Warnock, senior applications scientist at PMOD Technologies – a Bruker company, comments on the current state of play in PET image analysis:
"There is currently a tradeoff between obtaining detailed quantitative information and throughput. Researchers pursuing detailed analysis know that they won't be able to conduct many measurements due to time constraints, but sufficient throughput is important to keep the total cost of ownership for PET scanners down. We are constantly working to provide the cutting-edge hardware and software to support these quantitative studies and allow researchers to extract the most valuable statistical information from PET images."

Producing accurate quantitative data requires the manufacturer to supply adequate tools and quality control protocols, ideally in a user-friendly workflow. To support researchers interested in either fully quantitative analysis or simple analysis, Bruker offers dedicated software that extracts the most value out of PET images, and our in-house experts work with customers to match their individual needs with the right tools. PMOD is Bruker's software for fully quantitative PET image analysis, with a vast number of integrated tools for a range of applications including brain PET/MR analysis, kinetic modeling, cardiac PET and MR modeling and PET image segmentation.

Modern multi-modal technology

The concept of combining PET with MR has been around since the 1990s, but back then the technology faced limitations; fitting the PET hardware inside the MR scanner without impacting image quality was a challenge and, in the clinical space, PET/CT dominated. Now that the technology has matured, it is easier to integrate PET and MR in one instrument for simultaneous imaging, although PET/CT remains the simpler standard modality.

However, in contrast to PET/CT, PET/MR has enormous potential in both the clinical and preclinical space due to its enhanced soft tissue contrast capabilities. It can be achieved either by scanning the subject sequentially and later fusing the images by a software, or by hardware combination in simultaneous preclinical PET/MR systems. A recent study demonstrated the performance and MRI compatibility of a small animal PET insert (Bruker BioSpin), carried out with a Bruker BioSpec 94/20 MRI instrument, for simultaneous PET/MR imaging of mice and rats [12]. High spatial PET imaging resolution was achieved across the entire field of view (FOV), without any interference effects for PET and MRI. This allows researchers to obtain reliable quantification in their analyses.

A key advantage of simultaneous PET/MR imaging is the ability to match data both spatially and temporally – providing the unique opportunity to gain deeper insights into biological processes by combining the complementary information from PET and MR. PET/MR is a particularly powerful tool in preclinical neuroimaging, where obtaining high spatiotemporal resolution data can help researchers determine changes in neuronal activity with functional MRI (fMRI) and changes in receptor expression, neurotransmitter release, or metabolic demand with PET [13].

Dr. Peter Bruyndonckx comments on PET/MR:
"Many people believe that PET/MR is the future. It has advantages over PET/CT as it only contains one radiation modality. Combining PET with MR also enhances the capabilities to study detailed morphological changes in different organs and tumors, adding more precise information of the distribution and behavior of the PET tracer. Some examples of its uses are to detect changes in very small blood vessels or brain cell changes in dementia."

Current trends

Oncology

Quantitative tools like PET imaging are vital for obtaining physiological information about tumors, such as their metabolism, proliferation, necrosis, and hypoxic characteristics. Another major advantage of PET is its ability to provide information about tumor heterogeneity, which is especially important with regards to administering combination therapies for cancer.

A key characteristic of tumor cells is their elevated metabolic turnover, and ^{18}F-FDG is used to analyze glucose uptake in tumors to track their progression and to monitor aggressiveness.

Immuno-oncology is a rapidly evolving field, in which cancer patients are provided with more precise treatment that utilizes their immune system to tackle the tumor. Monoclonal antibodies (mAbs) against tumor-associated antigens have been shown to target tumors with high specificity and selectivity [14]. A growing number of mAbs are now being radiolabeled and evaluated for the detection of cancer and assessment of therapeutic response. For example, researchers recently identified a novel therapeutic target for prostate cancer, CD46, and developed the radiopharmaceutical compound [^{89}Zr] desferoximine (DFO)-YS5 for immuno-PET imaging using the Bruker Albira Si PET/SPECT/CT scanner [15]. This new immunoPET imaging probe, which showed specific binding to CD46 positive tumors in mice, has the potential for successful translation to the clinic as a theranostic platform and biomarker in prostate cancer.

PET imaging, in parallel with genomic profiling, could allow for visualization of drug-induced changes in a specific biochemical process, and could provide insights into drug target engagement or alterations in tumor phenotypes.

Neurology

PET imaging using ^{18}F-FDG has been applied to the differentiation of Alzheimer's disease (AD) from other neurological conditions for many years, but the growth in neurodegenerative disease research is driving the development of tracers that target relevant proteins such amyloid, tau, and synaptic vesicle 2A glycoprotein (SV2A). For instance, measuring SV2A in the brain with PET provides the potential for an *in vivo* biomarker of synaptic density and offers significant potential for a more accurate prediction of disease progression and the discovery of new treatment strategies [8].

Amyloid imaging agents such as Pittsburgh Compound-B (PiB) have long been used to provide information on the pathological and functional changes in the brains of AD patients which, together with ^{18}F-FDG PET, provides deeper insights into the relationships between amyloid deposition, cognition, and neurodegenerative processes [9]. More recently, researchers have explored the potential of fluorinated amyloid PET tracers, such as ^{18}F-florbetaben, ^{18}F-florbetapir and ^{18}F-flutemetamol, all three of which have been approved for clinical use by the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) [16]. These newer fluorinated amyloid tracers have a longer half-life (110 mins) than PiB (20 mins), improving their routine clinical application.

Various tau PET tracers have also been developed and used in preclinical studies but, unlike amyloid tracers, have yet to be validated for clinical use.

Pharmaceutical research

Successful drug development relies on the ability to understand dynamic biological processes, gene expression, enzyme and protein activity, progression and treatment of diseases, biodistribution, and pharmacokinetics/pharmacodynamics (PK/PD) of new drugs. Multi-modal PET imaging techniques, such as PET/MR and PET/CT, provide a method to label and follow the path of drugs throughout the body over time, to monitor efficacy and establish the drug's suitability for clinical use.

PET imaging can be a valuable tool for selection of the right drug candidates without labeling the drug itself. Drug activity can be estimated by PET receptor occupancy studies. By applying fully quantitative data analysis approaches, such as kinetic modeling, pharmaceutical researchers can answer critical questions, such as whether the drug has entered the brain, engaged its target receptor, and whether the dose level achieves sufficient receptor occupancy level for desired effects at an adequate therapeutic index.

For instance, a recent study [17] evaluated ^{18}F-UCB-H as a novel PET tracer for synaptic vesicle (SV) protein 2A in the brain. Fully quantitative microPET was used, and the selectivity of ^{18}F-UCB-H for SV2A was tested with the antiepileptic levetiracetam, which has been shown to directly target SV2A. The results indicated that ^{18}F-UCB-H is a selective tracer for SV2A *in vivo* in rats. PET imaging revealed a high degree of tracer binding in the brain and spinal cord, consistent with the known distribution of SV2A.

Future focus

Image reconstruction

In the clinical field, time-of-flight (TOF) PET has additionally helped to improve image quality and even reduce artefacts. TOF can establish the time difference in detection of the annihilation photons and therefore whether the annihilation was closer to one detector or the other. This information can be used in reconstruction, resulting in improved image quality. Although TOF is feasible in preclinical PET, the time resolution is too low to enable sufficient quality image reconstruction.

Dr. Josep Oliver. comments:
"Although TOF isn't practical in preclinical PET just now, we are working closely with key scientists in the clinical and preclinical fields to bring this technology to small animal imaging in the future.Another clinical trend that the preclinical field can learn from is total body imaging. Clinical total body scanners are now on the market but face a number of challenges, such as the need for improved corrections to account for the high number of randoms and scatter associated with regular doses. You can reduce the dose, but then have to accept a lot of noise. Bruker's PET scanners are inherently total body because the large FOV covers most of the animal, so we can learn from the refinements and corrections now taking place in clinical total body PET, to enhance reconstructions and corrections methods in the future. There is a nice degree of knowledge transfer between the clinical and preclinical fields, to collectively progress PET imaging capabilities"

Today, preclinical researchers have become accustomed to the high image quality possible with modern PET scanners. The challenge is obtaining such images at practical speeds. In the clinical space, machine learning (ML) is now being used to meet these demands, particularly when it comes to radiotracer dose reduction – a key trend driving future PET developments in clinical PET imaging. The potential of artificial intelligence (AI) to obtain the same quality images at lower doses is something which could take time to filter through to the preclinical space.

Dr. Josep Oliver explains:
"Preclinical researchers are skeptical of using technology that tells them what the image 'should' look like, rather than what is 'truly' there. We have always prioritized providing the correct data, and we continue to work hard to provide PET users with the image quality and performance that they need. It took researchers a long time to accept iterative reconstruction over analytical methods and much in the same way, it could be some time before they are ready to fully embrace AI. I think in the future it will find a place in several steps of image reconstruction, such as signal detection and de-noising, but not full image reconstruction in one step."

Dr. Peter Bruyndonckx also gives his thoughts on how AI could be utilized in certain applications:
"Previously in neurology, when imaging mouse brains, researchers used brain atlases from MRI and overlaid the PET image to see any changes. The brain is made up of such small structures that largely remain unchanged, so instead, we could train AI to recognize a mouse brain. Then when we inject isotopes, it will identify the differences without having to use a brain atlas."

Image analysis

Advances in total body PET in the clinical space are not only transferring to image reconstruction of small animal images but are allowing researchers to leverage multi-organ information with more complex image analysis models.

Given the throughput constraints of detailed quantitative PET imaging analysis, AI is poised to help with automatic analysis. Dr Geoffrey Warnock discusses where he sees the future heading: "At the moment, we're seeing a resurgence in AI. But AI is the prototypical black box that researchers are trained not to rely on, and researchers should question what is happening in that box. I think the future of PET image analysis will be a division between fully automated processing of the simpler tasks with AI, while keeping an eye on the black box. We need to maintain the knowledge of fully quantitative PET, as this is where preclinical researchers can extract the most value."

Dr. Geoffrey Warnock comments on the potential use of these models for multi-organ kinetics:
"To really make the most of total body PET, we will need more complex mathematical models to extract multi-organ information, such as metabolism. What we have found is that trends in the clinical sphere, for example using PET to diagnose and monitor neurodegenerative disease, can lead to funding for preclinical research. We then have this cycle where breakthroughs as a result of this research lead to more advanced treatments for dementia."

Conclusion

Preclinical imaging plays a vital role in developing our understanding of the biological processes behind disease states at the organ, tissue, cell and molecular level. Using PET imaging in preclinical studies enables users to conduct repeat experiments on the same animal subjects, providing strong statistically valuable data and therefore reducing the number of animals required for a study. It has therefore become increasingly important to use non-invasive *in vivo* imaging techniques to study diseases.

Since the launch of the first small animal scanners in the 1990s, PET hardware and image reconstruction and analysis tools have advanced to meet the evolving needs of preclinical researchers. Many of these developments have occurred in parallel with clinical PET imaging, and the transfer of knowledge between the two fields has helped the technology's innovation as a whole.

Multi-modal tomographs, such as PET/CT, allow the correlation of the functional imaging obtained using PET with the anatomic imaging obtained with CT scanning. PET/MR is gaining ground in preclinical imaging applications, as it offers superior soft tissue contrast, imaging without the CT's ionizing radiation risk, as well as multiparametric information.

Preclinical research applications, such as oncology and neurology, have benefited from advances in tracer development, image reconstruction, and image analysis. Bruker's team of PET experts works closely with researchers to develop and test new technologies to propel imaging forward, opening new opportunities from previously unreachable data.

About the Author

Mette Lauritzen, PhD, joined Bruker BioSpin in 2020 as Market Product Manager for Nuclear Molecular Imaging. She has an academic background in preclinical MRI and PET Imaging, having completed post-doctoral positions at the Danish Research Center for Magnetic Resonance (DRCMR) and Stanford University, School of Medicine's Radiology Department.

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- PMOD biomedical image quantification software offers fully quantitative PET image analysis, with a vast number of integrated tools for a range of applications including brain PET/MR analysis, kinetic modeling, cardiac PET and MR modeling and PET image segmentation

About the contributors

Peter Bruyndonckx, PhD., is a principle scientist for micro-CT and system architect for Nuclear Molecular Imaging at Bruker. He joined Bruker in 2008 after a 15-year academic career as a detector physicist, focusing mainly on the development of preclinical PET instrumentation technologies. During that period he also pioneered the use of monolithic scintillator based PET detector, combined with machine learning positioning algorithms.

Josep Oliver, PhD., joined Bruker BioSpin in 2019 as senior image reconstruction expert for nuclear molecular imaging. He has an academic background in theoretical physics and more than ten years of experience in preclinical imaging focusing on reconstruction methods for PET and Compton cameras.

Geoffrey Warnock, PhD., is Managing Director of PMOD Technologies LCC, a Bruker company since 2019. He has worked in imaging for more than 10 years, with experience in both small animals and humans, and a focus on fully quantitative PET. He was involved in the development and evaluation of ^{18}F-UCB-H for synaptic vesicle glyco protein 2A, and more recently in first-in-man studies with ^{18}F-PSS232 for mGluR5. Having initially trained as a pharmacologist, Geoff can combine a strong understanding of the biological underpinnings to imaging with extensive hands-on experience of imaging in clinical and preclinical research.

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