Advantages and Applications of Total-Body PET Scanning

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Total-body positron emission tomography (PET) scanning can not only image faster than traditional techniques with less administered radioactivity but also perform total-body dynamic acquisition at a longer delayed time point based on its ultrahigh detection sensitivity, enhanced temporal resolution, and long scan range (194 cm). These unique characteristics create several opportunities to improve image quality and can provide a deeper understanding regarding disease detection, diagnosis, staging/restaging, response to treatment, and prognostication.

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1. Introduction

Over the past few decades, researchers around the world have been intent on improving the sensitivity and resolution of positron emission tomography (PET) imaging. Recent modifications include the introduction of novel gating methods, iterative reconstruction algorithms, detectors with optimized geometry, time-of-flight technologies, and integration of computed tomography (CT) imaging. While these changes have remarkably improved PET quality, the limited axial coverage of current PET scanners continues to be a significant constraint in the face of current imaging systems. With an axial coverage of 15–30 cm, PET detectors ultimately collect a limited number of coincidence photons, thus generating images deemed too noisy given low counting statistics.

To overcome these limitations, total-body-length PET scanners were developed, thus extending the axial field of view (AFOW) to cover the entire human body. In addition, by increasing the number of detectors, most emitted photons can be captured, thus dramatically increasing sensitivity, and allowing for simultaneous dynamic acquisition from all tissues of interest. Ultimately, this ultrasensitive high-performance device offers many advantages over conventional systems, such as an enhanced signal-to-noise ratio (SNR), image quality with a shorter acquisition time, and lesser injected radioactivity.

2. Major Advantages of Total-Body PET Scanners

2.1. Increased Signal-to-Noise Ratio

While the radiation exposure associated with PET/CT imaging often presents as a major concern, many characteristics associated with the total-body scanner can ease the radiation burden. For instance, the ultrahigh

sensitivity offered by the total-body scanner allows it to provide comparable images with remarkably lower activity. This can be attributed to the signal-to-noise ratio, which is directly correlated with the sensitivity of the scanner, acquisition time, and activity administered. The SNR value also determines the image quality, with a higher SNR indicating a higher-quality image. Thus, total-body scanning's high sensitivity (up to 68 times higher than PET/CT), even in the setting of lower administered activity, will still yield an increased SNR value and allow for a 40-fold reduction in radioactivity dose [1]. Lower activity also reduces dead-time count loss, thus further improving image quality [2]. Ultimately, lower administered activity can enable previously vulnerable populations such as young children and pregnant women to utilize PET/CT technology.

2.2. Reduction in Imaging Time

One of the primary benefits associated with total-body scanning is the reduction in imaging time. Certain authors have estimated that this imaging technique decreases length in imaging by a factor of 24 [1]. Thus, a 12-min multiple-bed-position study can be performed in a single-bed position in under 30 s with comparable image quality, and the entire scan only taking 5 min. Imaging faster has a variety of benefits, such as reduction in respiratory motion, elimination of the need for sedation in certain patient groups, and enhanced patient throughput per unit of time in a single workday. In addition, imaging young patients or patients with pain or claustrophobia becomes vastly easier and more comfortable [3].

2.3. Ultrafast Acquisition for Motion Correction

Another benefit of total-body scanning involves the shorter acquisition time, thus resulting in less movement-induced blurring and allowing for ultrafast breath-hold equations to correct signal processing in moving regions. This is primarily due to this ultrafast tool's ability to image in a single breath-hold, thus reducing respiratory motion artifacts and consequently improving target quantitation and localization on PET/CT imaging [4].

2.4. Detectability of Smaller Lesions

A major flaw associated with conventional fluorodeoxyglucose (FDG)-PET/CT technology involves its inability to detect metastatic deposits smaller than 5 mm due to its limited sensitivity. Total-body scanners, on the other hand, with ultrahigh sensitivity, good spatial resolution, and a long scan range, can detect small, low-density tumor deposits and micro-metastases. In addition, the high lesion SNR makes it possible to detect small lesions near the diaphragm affected by respiratory artifact.

2.5. Total-Body Dynamic Scanning

In order to extract quantitative parameters from the temporal analysis of the radiotracer distribution in voxels, novel four-dimensional (4D) dynamic whole-body PET acquisition methods have been suggested [5][6]. After extracting the plasma input function from the acquired images, this method utilizes a Patlak-based modeling approach to provide an estimation of kinetic parameters such as the tracer uptake rate K_i (slope) [7]. Certain authors have recognized the superiority of this 4D dynamic over the traditional three-dimensional (3D) approach in tumor

characterization and distinguishing inflammation versus malignancy [8]. However, the early studies evaluated this dynamic PET methodology using a one-step conventional system (15–20 cm), which limited its ability to assess multiorgan diseases (cancer and beyond). Thus, multistep dynamic PET acquisition protocols have been tested and note various strengths and limitations.

2.6. Longer Acquisition Delay

Another benefit of total-body PET scanners is that the study can be obtained at much later time points after tracer injection, thus enhancing the contrast between the tumoral lesion and background tissue. Certain authors, such as Price et al., even note an increase in contrast between tumor and background tissue of approximately 4-fold if the interval between administration of FDG is increased [9]. This can be explained by a wider distribution of radiotracer on delayed images, greater accumulation in the tumor, renal excretion, and a greater washout from normal tissue [10]. Thus, images obtained with a longer delay may reveal additional information about the extent of disease and enable visualization of smaller or less tracer-avid lesions not seen on prior imaging [11].

2.7. Detection of Distant Metastases and Vascular Complications

Whereas conventional whole-body PET/CT might miss distant metastases due to its limited scan range (that is, head to thigh), total-body PET can cover the entire body (head to toe) in a single bed position. While distal metastases in the lower extremities are oftentimes rare in most adult-onset malignancies, due to the lack of red bone marrow in an adult's lower extremities, this technique may be beneficial in the pediatric population.

3. Multiorgan Diseases

3.1. Oncologic Applications

The high sensitivity and dynamic range of total-body PET imaging allow for imaging at much later time points post radiotracer injection (up to 5–6 half times). This is particularly important as tumor contrast typically increases with time, given the clearance of tracer from other tissues. For example, most malignant lesions, including primary cancers and metastatic lesions, would show higher FDG uptake 2 h post-injection rather than 1 h. Thus, delayed imaging can add vital information regarding disease extent by enhancing tumor uptake and detecting smaller or lesser-avid lesions [12][13].

3.2. Non-Oncologic Applications

Obesity and metabolic syndromes: Total-body PET imaging coupled with various metabolic tracers and advanced modeling techniques has great potential in the field of metabolic disorders. These techniques can enable both clinicians and researchers to investigate the pathophysiology of obesity-related metabolic disorders, and therefore contribute to the development of targeted interventions [14].

Total-body PET imaging also has great value in monitoring and detecting atherosclerotic disease, as current imaging techniques have a variety of limitations [1]. For instance, traditional structural imaging techniques are of limited utility in the prediction of plaque rupture. Standard PET techniques generate images with a suboptimal number of counts and thus a greater amount of noise [1]. Total-body scanning, on the other hand, can decrease the administered dose, delay acquisition, and reduce the scan time. This is turn would allow for serial monitoring in this patient population while still minimizing radiation exposure [1].

4. Miscellaneous Applications of Total-Body PET in Clinical Practice

Differentiating between Residual Disease and Post-Therapy Changes

A major flaw associated with traditional anatomic imaging techniques such as CT scans or magnetic resonance imaging (MRI) is that these methods cannot reliably distinguish residual disease and post-therapeutic sequalae (such as post-surgical or post-radiation changes), thus generating false-positive cases. While conventional FDG-PET/CT holds a powerful diagnostic ability in this arena, a 3-month interval is still required post-therapy to minimize the likelihood of false-positive results.

Another flaw inherent in traditional FDG-PET/CT studies involves its inability to differentiate pseudo-progression and confirmed progression. This in turn can be misleading for clinicians analyzing response to treatment with systemic immunotherapy.

5. Drug Development

Other authors have identified a promising niche for total-body PET/CT imaging in drug development. Currently, many laboratories utilize animal models to conduct pharmacokinetic and pharmacodynamic studies, but these models are fraught with limitations. In order to combat this, micro-dosing methods have been developed using highly sensitive imaging tools (such as single-photon emission computed tomography (SPECT) and PET) to introduce novel therapeutic agents to humans [15][16]. Micro-dosing ultimately facilitates drug development by initiating human involvement prior to phase I trials, thus hastening the decision-making process by quickly removing ineffective compounds from the drug pipeline [17].

6. Monitoring Cellular and Nanoparticle-Based Therapies

Recently, novel therapeutic strategies such as cell-based therapies (e.g., adoptive immunotherapy and stem-cell therapy) have attracted substantial attention in the field of oncology. To facilitate the development of these nanoparticle-mediated therapies, a reliable assessment tool with high sensitivity such as total-body PET technology is necessary to determine the in vivo distribution and biological fate of injected substances [18].

To this aim, labeling cells with long-lived radionucleotides prior to injection has been standard practice in the realm of nuclear medicine. After cell labeling, various noninvasive imaging modalities are applied to visualize these cells or nanoparticles in vivo, as well as monitor and quantify cell accumulation and function.

7. Multi-Tracer PET Studies (Cocktail Injection)

While FDG-PET/CT technology plays a pivotal role in imaging certain cancers, several malignant lesions cannot be detected using FDG due to the variable rates of glucose metabolism present in some cancers. To overcome this limitation, the novel strategy of cocktail injection has been developed, in which two radiopharmaceuticals are combined prior to a single PET acquisition [19].

8. Personalized Medicine

Over the past decade, traditional medicine has been rapidly shifting to the concept of personalized medicine, including molecular targeted therapy, immunotherapy, and theranostics. These personalized medicine techniques have been highly successful in the field of clinical oncology, where clinicians can evaluate specific tumor markers and select patients who might benefit from a specific molecular-targeted therapy, thus maximizing the therapeutic effect and minimizing toxicity [20]. Consequently, certain advanced, automated software such as radiomics has been developed to extract more data from image-based features [21].

In addition to highlighting imaging biomarkers related to intratumor heterogeneity, PET radiomics may also be useful in novel therapy paradigms such as immunotherapy, somatostatin receptor (SSTR) therapy, or prostate-specific membrane antigen (PSMA)-targeted theranostics. The potential usefulness of PET radiomics for personalized medicine has been widely reported in various cancers [22][23][24], as it allows for tumor marker evaluation, response prediction, and prognostication.

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