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POSITRON EMISSION TOMOGRAPHY AND PATIENTS' QUALITY OF LIFE

Abstract: *The design of new medical devices has the potential to improve the outcome of many diseases by changing the way they are diagnosed and monitored. Positron emission tomography (PET) provides insight into the body's metabolic processes, allowing for precise visualization and quantification of tissue activity. Available evidence shows a strong impact of this imaging modality in various diseases. PET can play a key role in personalizing therapy based on molecular characteristics, which contributes to reducing adverse effects, improving treatment outcomes, but also improving the quality of life of patients. Assessing the quality of life and mental state of patients is of vital importance for clinicians as well as for the patients themselves.*

The aim of the paper was to highlight and further improve the understanding of progress in the development of the medical device design process, with a focus on current progress and future opportunities in PET design and its impact on the quality of life of patients.

Keywords: *design, medical devices, positron emission tomography, quality of life.*

1. Introduction

Medical imaging plays an important role in clinical analysis and disease diagnosis by providing visual representations of a subject's internal structures and/or physiological processes hidden beneath the skin. In addition, it allows for the establishment of a database with thousands of anatomical and physiological images. The emergence of these databases has become significant for the training of physicians and new machine-based systems to identify abnormalities.

Positron emission tomography (PET) is a functional imaging technique based on the use of a radionuclide that, upon decay, emits positrons, i.e. positively charged subatomic particles with a mass equal to that of an electron. In recent years, PET has become one of the most powerful tools for obtaining functional images due to its high sensitivity to differences in metabolic and biological activities at the molecular level. It is currently used in a wide range of clinical areas, such as oncology, neurology, and cardiology (Rohren et al, 2004).

PET significantly improves the quality of life of patients through accurate diagnosis, early detection of diseases and optimization of treatment plans. Thanks to its high sensitivity to metabolic changes in the cell, PET allows for the early detection of malignant tumors, neurodegenerative diseases and cardiovascular problems, which increases the chances of timely and effective treatment. In addition, PET helps monitor the response to therapy, allowing for adjustments of therapy to the individual

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needs of patients, thereby reducing the side effects of therapy. By making the diagnosis more precise, PET reduces stress and uncertainty in patients, improving quality of life and disease outcome (Evangelista & Morigi, 2023).

In order to improve diagnostics and develop multimodality systems for functional and anatomical imaging, PET has been integrated with other techniques such as computed tomography (CT) and magnetic resonance imaging (MRI). Although the integration of PET and CT is already widely accepted, PET/MRI systems have taken longer to develop due to the limitations of photomultiplier tube detectors. Thanks to advances in photosensor technologies in recent years, PET/MRI systems have become available and used in many clinical applications. It has become clear that the selection and optimization of technology, methodology and concept are crucial for the overall performance and integration of PET in biomedical research and healthcare. This includes scanners with much greater geometric body coverage, highly sensitive and compact silicon photomultiplier sensors, fast PET detectors (time of flight -TOF) that use traditional scintillation light or other fast emissions, and fast electronics combined with computational methods to better estimate the locations, timing, and energies of interactions in the detector (Zaidi et al, 2011).

The aim of the research was to highlight and further improve the understanding of progress in the development of the medical device design process, with a focus on current progress and future opportunities in positron emission tomography design and its impact on patients' quality of life. A comprehensive and detailed search was conducted using the keywords "design", "medical devices", "positron emission tomography", "quality of life" in PubMed, Google Scholar and ScienceDirect databases to determine eligible studies.

2. Specificities of medical devices

2.1. Definition of medical devices

Medical devices encompass a wide range of technologies and are an integral part of modern healthcare settings. Their application contributes to the improvement of healthcare, enabling more precise diagnostics, monitoring of patient conditions, and more effective medical interventions (Miclăuş et al, 2020). Accordingly, the first starting point in learning about medical devices is to understand what a medical device is. The Working Group on Global Harmonization defines a “medical device” as any instrument, apparatus, material or other product, whether used alone or in combination, including the software necessary for its proper application, intended by its manufacturer for human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation or compensation for injury or disability,
- examination, replacement or modification of anatomy or physiological process,
- birth control,

which does not achieve its primary targeted effect in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function in this way.

In addition to this definition, one can often hear an equivalent definition from the Food and Drug Administration (FDA), according to which the term "device" means an instrument, apparatus, tool, machine, invention, implant, in vitro reagent, or other similar or related product, including any component, part, or accessory, that is:

- recognized in the official national formulary, or the United States

Pharmacopoeia, or any supplement thereto,

- intended for use in the diagnosis of disease or other conditions, or in the treatment, mitigation, or prevention of disease in humans or other animals, or
- intended to affect the structure or any function of the human body or animals, and which does not achieve its primary effects by chemical action in or on humans or animals and which is not metabolized to achieve its primary purposes (Kelly & Jones, 2018).

Both definitions clearly distinguish a device from a pharmacological agent, with the only difference being the inclusion of the use of medical devices on any animal in the FDA definition.

The medical device industry is rapidly evolving through technological disciplines such as biomaterials science, electronics, microtechnology, and nanotechnology (Ogrodnik, 2020). Some notable medical devices include catheters, dressings, tomography machines, long-lasting surgical implants, magnetic resonance imaging machines, X-ray machines, surgical gloves, artificial hips and knees, hemodialysis machines, ultrasound scanners, positron emission tomography machines, and many more.

2.2. Characteristics of medical devices

Medical devices, encompassing a wide range of products, must be carefully designed and manufactured to meet the specific requirements of diagnosing, treating, and monitoring patients. The characteristics of medical devices vary depending on the type of device, but in general, some of the key aspects that characterize medical devices include:

1. Safety - Medical devices must meet high safety standards to protect users and patients. This includes analyzing potential risks and implementing protective measures.
2. Efficacy - A medical device must fulfill its intended purpose efficiently and accurately. The ability of a medical device to provide an accurate diagnosis or appropriate therapy is one of the key characteristics.
3. Quality - The quality of manufacturing and materials is essential to ensure the reliability and durability of medical devices.
4. Design - The design of medical devices should be adapted to the purpose and users.
5. Ergonomic design can improve usability and safety.
6. Regulatory compliance - Medical devices must comply with relevant regulations and standards to ensure compliance with legislation.
7. Appropriate labeling – medical devices often require appropriate labeling and information to inform users of their purpose, method of use, and other relevant information (French-Mowat & Burnett, 2012).

High levels of functionality, precision, safety, and adaptability to new technologies are becoming the cornerstones of the efficient and safe application of biomedical devices. Innovations in design, device connectivity, and adherence to strict regulatory standards contribute to the creation of devices that not only facilitate the work of healthcare professionals and improve diagnostics, but also provide patients with safer and more personalized treatments. Through continuous improvement and adaptation to technological innovations, the characteristics of medical devices play an important role in shaping the future of healthcare, setting the standards for high-quality and safe medical practice.

3. Medical device design process

3.1. Analysis phase

The analysis phase of the medical device design process involves a detailed study of requirements, identification of objectives and constraints, analysis of user needs, and risk assessment. Problem analysis and specification during the analysis phase of the medical device design process represent key steps that lay the foundation for successful development.

3.2. Synthesis phase

The synthesis phase in the medical device design process is the step in which various components, information, and requirements are combined to create a complete and functional solution. This involves integrating medical needs, technological aspects, ergonomics, materials, and regulations to achieve appropriate device efficacy and safety.

3.3. Evaluation phase

The evaluation phase is a link in the medical device design process that ultimately allows for the assessment of the performance, safety, and functionality of the proposed solution before it is put into production and implementation. This phase includes a series of activities that ensure that the final product meets the set standards, user needs, and regulations. The ultimate goal is to ensure that the medical device meets the highest standards of quality, safety, and efficacy before it is made available to users.

4. Methods of design of medical devices

In recent years, increasing innovations in the field of design development of various types of medical devices have aimed, first of all, to improve diagnostic results, but also to improve treatment and the process of monitoring the health conditions of patients. When it comes to the goals themselves, the idea is to increase the accuracy of disease diagnosis, reduce risks and improve the overall efficiency of the healthcare system. However, in order to achieve effective and useful innovations, it is necessary to apply some design method. In the field of medical technologies, two key design methods can be identified, the so-called new and traditional methods. The combination of these two methods allows for great adaptability and significantly affects the speed of innovation, while maintaining a high standard of safety and efficiency (French-Mowat & Burnett, 2012).

4.1. Traditional methods of medicine devices design

The following will list the most popular traditional medical device design methods with a brief explanation of each individual method:

- Waterfall Model: This method is often used when the requirements for the innovation are well defined and there is less likelihood of changes during the development process. What is important to note is that this model has a linear approach that requires precise definition of requirements at the very beginning of the innovation development process, after which each development phase (design, implementation, testing) is performed one after the other.
- V-Model: This model has similarities with the previously mentioned method, however, the idea of this method is focused on testing the project at each development phase. This practically means that each development phase has its own corresponding testing phase, thus ensuring quality

throughout the development process.

- Iterative Model: This method allows for the re-execution of certain development phases through iterations in order to improve that phase and adapt it to the feedback received. This approach contributes to great flexibility throughout the development of medical devices.

4.2. New methods of medical devices design

Below are the most popular traditional medical device design methods with a brief explanation of each individual method:

- Agile approach: This approach involves working in short iterations with a clear goal, which is to achieve a high level of user satisfaction. This method has proven to be very useful in situations where requirements are variable or poorly defined at the very beginning of the project.
- Design-thinking: The focus in this method is on the user experience and solving real problems that users face. For this reason, this method is very important for medical device designers. The very idea of the method is based on understanding all user needs and creating a solution that is easily acceptable for both patients and healthcare professionals.
- Incremental and spiral models: Simply put, the incremental model adds new value and functionality in small iterations, i.e. steps, thus enabling the rapid delivery of the required innovation. On the other hand, the spiral model includes risk analysis, planning and iteration, which is especially useful when changes are expected during the development phase of the process.
- Use of advanced technologies: Due to the rapid progress of the technology industry, the use of advanced technologies in the design of medical and many other devices has become increasingly intensive in recent years. The aim is to integrate artificial intelligence, introduce the concept of "internet of things (IoT)" and 3D printing, which allows medical device designers to even improve performance, increase the accuracy of disease diagnostics and fully optimize the necessary treatments.

5. Positron emission tomography

For whole-body imaging or targeted imaging, after the introduction of a selected radiopharmaceutical into the patient's body, standard PET scanners are used, and more recently, hybrid PET/CT or PET/MRI scanners. Specially designed PET devices are also used for the diagnosis of diseases of certain organs, as well as for the experimental application of this technology in animals (Cherry et al, 2012).

PET devices consist of a detector system and a computer system for image reconstruction. What causes scintillators in the PET detector are penetrating gamma photons that are produced at the point of stopping and disappearing (anchilation) of the positron. After losing most of its energy in several collisions with electrons in the tissue, the positron annihilates together with one electron from the tissue, with their mass being transformed into energy in the form of two gamma photons of 511 keV each (Surti, 2015). Detectors surrounding the patient collect 107 to 108 decay events, which are then used to reconstruct a PET image that reflects the distribution of radionuclides in the body. Very often, one or even both of the anchilation photons will scatter around the patient and change direction, losing some of their energy, referred to as scattered events. There is the possibility of random events, where two photons from unrelated radionuclide decays hit the detectors at almost the same time, which would seem to produce a valid case of coincidence. However, the number of scattered and random events should be minimized to obtain the highest quality images. Ultimately, the two annihilation photons will arrive at the detector at slightly different times depending on the distance each annihilation photon has to travel from its production site to the detector. The ability of a PET scanner to measure this time difference is called PET time-of-flight, and time-of-flight information in image reconstruction helps localize the event and improve image quality (Surti, 2015).

The basic detection unit used in almost all PET scanners is the scintillation detector, which consists of a dense scintillator crystal connected to a sensitive light detector (photodetector). The main function of the PET detector is to collect three types of information – the position where a gamma photon strikes the scintillator, the time when the output pulse from the photosensor arrives, and the energy of the output pulse. On the other hand, the photodetector in the PET detector plays a very important role in terms of spatial resolution, temporal resolution, and energy resolution (Jones & Townsend, 2017; Muehllehner & Karp, 2006).

A number of small scintillation crystals in the PET scanner detector, shaped like a quadrangular prism, are arranged in a circle around the aperture in which the patient is located during acquisition. The crystals are grouped into blocks, equipped with photomultipliers connected in a network to determine the position of anchilation within the detector's field of view.

Each simultaneous (coincident) detection of two 511 keV photons at different locations in the ring is recognized by the system as an anchilation, and the positions of the excited crystals in the detector determine the direction of the line on which anchilation occurred. In this way, electron collimation is achieved (Ota et al, 2017).

Looking at the development of PET scanners, one can see that performance has improved dramatically. Initially, single-ring cameras were used, but they were later replaced by multi-ring cameras, which, together with brighter and faster scintillators and more sensitive photodetectors, significantly improved spatial, energy, and temporal resolution. In addition, simultaneous advances in electronics and computing have played an important role in the production of clinical PET scanners, which have become much better than those of a few decades ago. Standard clinical PET scanners have come quite close to a consistent design, with scintillator crystals measuring 3x3x20 mm, coupled with sensitive photodetectors (Rausch et al, 2019; Wanarak et al, 2012). As for the photodetectors themselves, they are most often silicon photomultipliers or photomultiplier tubes. Lutetium-based scintillators, such as lutetium orthosilicate (LSO) and lutetium yttrium orthosilicate (LYSO), are used in almost all modern systems due to their favorable stopping power, good brightness, and short decay time, resulting in high sensitivity, fast time resolution, reasonable resolving energy, and low dead time. Due to their compact size, magnetic insensitivity, and high photon detection efficiency, silicon photomultipliers are the photodetectors of choice for modern PET scanners (Renker, 2007). Silicon photomultipliers are a type of solid-state detector composed of several thousand individual microcells, each of which emits an avalanche of charges in response to a detected optical photon. Typically, microcells are connected in parallel and can therefore also be used as photon counting devices. A special type of silicon multiplier is the so-called digital silicon multiplier, which has numerous practical advantages, such as the ability to disable extremely noisy microcells and flexible digital processing circuits (Schaart et al, 2016).

The main trends in detector development generally include improving the generation and collection of scintillation light using more modern scintillators and photodetector technologies. In addition, in order to improve the use of information contained in the photodetector waveforms, work should be done to optimize the detector configuration and develop new signal processing algorithms. In order to form powerful hybrid diagnostic devices, most PET scanners have the ability to TOF reconstruction or are integrated with CT or MRI.

5.1. PET/CT and PET/MRI systems

Dual-modality imaging systems, such as PET/CT and PET/MRI, reduce patient scanning time and allow simultaneous acquisition of images in the same bed position, reducing registration and image fusion errors and providing more information for diagnosis. PET/CT systems have been widely used in many preclinical and clinical areas for decades, while PET/MRI systems have only recently gained popularity due to the limitations of the photomultiplier tube in a magnetic field. However, with the technological advancement of solid-state sensors such as the silicon photomultiplier, many PET/MRI imaging systems have been designed and developed (Vandenberghe & Marsden, 2015).

The first commercial digital PET/CT with improved TOF performance was offered by Philips Version. The basic detector consisted of a digital photon counter and a 4x4x19mm3 LYSO scintillator array connected to the digital photon counter by direct coupling. Due to the significantly improved performance of the digital photon counter, Philips achieved better spatial, temporal, and energy resolution (Queiroz et al, 2018). Interestingly, the latest PET/CT system from Toshiba is still based on photomultiplier tube technology. The detector is made of a multiplier tube and a lutetium-based scintillator, and the system achieved temporal, spatial, and energy resolution comparable to PET systems based on solid-state sensor technologies such as the silicon photomultiplier (Zaidi et al, 2011). Hybrid PET/MRI devices have significant advantages in the diagnosis of numerous diseases, with numerous advantages over PET/CT devices. First and foremost, MRI is based on the use of non-ionizing radiation, which significantly reduces the radiation burden on the patient. In addition, PET/MRI systems benefit from the advantages of both imaging modalities. PET can provide functional imaging that shows metabolic processes, while MRI shows excellent soft tissue contrast. Although PET/MRI has many advantages, the biggest problem in the design of this device was its incompatibility with magnetic fields. Therefore, PET systems based on photomultiplier tubes could only be combined with MRI systems using additional technology. On the other hand, solid-state sensors are compatible with magnetic fields, which has accelerated the development of hybrid PET/MRI modalities (Zaidi et al, 2011). The design of the PET/MRI device itself is based on the installation of the PET and MRI systems face-to-face separately, and a movable table between the PET and MRI is used to move the patient to different systems for image acquisition. The Ingenuiti TF PET/MRI whole-body imaging system uses photomultiplier tube technology in its hybrid system. In order to avoid mutual system interference, especially magnetic field interference, a magnetic shield has been introduced into the design of the PET gantry (Pichler et al, 2008). There are also systems based on silicon photomultiplier technology that is compatible with magnetic fields, such as the SIGNATM PET/MRI hybrid systems. This PET/MRI system does not require a special design of the PET system protection and compared to the

Ingenuiti TF PET/MRI system, one of the advantages is that it is a simultaneous system, which acquires PET and MRI images at the same patient position at the same time. This results in reduced scanning time and improved accuracy for co-registration and fusion of PET and MRI images (Zaidi & Alavi, 2007).

6. Conclusion

In conclusion, medical device design plays a crucial role in improving diagnostic capabilities and therapeutic interventions. Through a review of various design aspects, the importance of integrating innovation, ergonomics and efficiency in improving the quality of medical care can be seen. The use of PET as a highly sophisticated imaging method allows for precise visualization of metabolic processes in the body. Accordingly, the continuous development of PET contributes to a comprehensive understanding of the pathophysiology of diseases and a personalized approach to treatment. Continuous research and development in the field of medical device design is necessary to achieve better results in medical practice. Also, collaboration between engineers, medical staff and researchers is essential to ensure that new devices meet the real needs and challenges in the medical environment. The combination of innovation in design and the application of advanced technologies, such as PET, promises a bright future in the field of medical diagnostics and therapy.

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