Assessing Metastasis through Positron Emission Tomography (PET): An In-depth Analysis and Mapping of Thematic Clusters and Prevailing Topics in Nuclear Medicine Research

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ABSTRACT

Objective: The primary objective of the study is to conduct a critical evaluation of thematic categories within the field of nuclear medicine literature, specifically focusing on positron emission tomography (PET) imaging techniques and the detection and evaluation of metastasis, through the application of bibliometric analysis methods.

Method: Co-citation, co-occurrence and co-authorship analyses were performed on 588 academic publications selected using the Web of Science database. The analyses were performed using R-based Bibliometrix software, Python and Microsoft Excel.

Results: The findings derived from the co-citation and co-occurrence network analyses shed light on the intricate nature of thematic categories within the nuclear medicine literature and provide insights into the core topics. Topics such as metastasis and tumor staging, optimisation of imaging methodology, and standardisation of clinical practice are prominent topics in the study. In particular, a single-authored article has been observed to make a significant contribution to knowledge on the efficacy of different radioactive markers used in the diagnosis of neuroendocrine tumors.

Conclusion: This bibliometric assessment addresses the multidisciplinary and thematic dimensions of an in-depth understanding of the field of nuclear medicine. The study effectively identified four main thematic clusters ‘PET and Cancer Types’, ‘FDG-PET’, ‘Prostate Cancer and Recurrence’, and ‘Cancer Management and Imaging’ and highlights the interrelatedness and importance of these categories.

Keywords: Bibliometric Analysis, Nuclear Medicine, PET Imaging, Metastasis Detection, Thematic Clustering, Metastatic Disease Management, Health Policy, Economic Impact, Clinical Utility, Technological Advancements.

INTRODUCTION

Nuclear medicine plays a pivotal role in the diagnosis and management of critical health issues, such as metastasis and tumor staging. Particularly in cases of oncological disorders, this medical discipline holds paramount importance for early detection and continuous monitoring of metastasis. Among the various nuclear medicine applications, Positron Emission Tomography (PET) stands out as a highly sensitive imaging technique capable of detecting metastasis. The advancement of medical imaging technologies, notably Positron Emission Tomography (PET), significantly impacts the decision-making processes of healthcare professionals (1,2).

Nonetheless, the literature within this field is both extensive and intricate, with a multitude of techniques and applications further contributing to this complexity (3–7). Additionally, PET imaging plays a crucial role in the identification of metastatic diseases, particularly in cases of bone metastases (8–12).
The importance of imaging techniques in cancer diagnosis has been increasing, especially in recent years. Different imaging modalities such as positron emission tomography (PET) and computed tomography (CT) have high diagnostic value in the diagnosis of specific cancer types (13,14). Furthermore, the effectiveness of imaging techniques is high for specific cancer types such as prostate cancer and bone metastases (15–17). Comparison of the diagnostic performance of different imaging techniques is also frequently discussed in the literature (18–20). Furthermore, advanced technologies like radiomics and automation have demonstrated their effectiveness in cancer diagnosis (21,22). However, these studies have generally focused on specific cancer types or metastasis sites, so more extensive research is needed. Early and accurate diagnosis of metastasis is critical for the effectiveness of cancer treatment processes. Therefore, imaging techniques and advanced technologies in cancer diagnosis are expected to contribute to a holistic assessment of metastasis.

Metastases occur when cancer cells spread from the primary tumor to a different organ or tissue. Early detection and monitoring of this process is critical for treatment. Different imaging technologies are used to detect metastases. For example, Mazzola et al (23) compared two PET-CT methods in prostate cancer. Evangelista and colleagues (24) found PET/CT and CT to be useful in the early detection of bone marrow metastases. Gwak et al. (25) showed that radiosurgery planning can be done with F-18-fluorodeoxyglucose PET. Metastasis patterns can vary depending on the type of cancer; for instance, in the case of lung cancer, factors such as age and histologic subtype may exert an influence on these patterns (26). These studies emphasise the importance of imaging technologies for metastasis detection and treatment planning. In conclusion, the efficacy and comparative advantages of different imaging modalities in the diagnosis and management of metastases have been examined in various studies. This is critical for early detection and effective treatment planning. Nevertheless, conducting comparative assessments of these technologies and identifying the specific conditions for which they are most suitable necessitates additional research.

The objective of this study is to perform a bibliometric analysis of literature within the domain of nuclear medicine, with a particular emphasis on PET imaging techniques and the detection and evaluation of metastasis. Through the application of the co-citation analysis method, various themes, clusters, and sub-themes have been identified in this research. Significantly, this form of bibliometric co-citation analysis has not been previously conducted within this field. This approach has the potential to offer a comprehensive and profound insight into the literature, serving as a foundation for future research endeavors in this domain.

In this study, the topic of positron emission tomography (PET) and metastases in the field of nuclear medicine was examined, particularly through bibliometric analysis. The following research questions have been identified to delve deeper into the relationship and dynamics between PET and metastasis. Our objective is to conduct a thorough evaluation of academic advancements in the PET and metastases field and pinpoint subjects that can steer future research endeavors. In this framework, the study addresses four main questions.

- Who are the most prolific authors, the most cited journals, institutions and countries, and the most cited papers in PET and metastasis, and what are the most commonly used words?
- What are the most critical classic studies in PET and metastasis? What are the dynamics in the evolution of the intellectual landscape of PET and metastasis?
- What themes has the field of PET and metastasis enabled the development of? What are the prominent themes and the critical issues emphasised in these themes?
- Can a list of the most common metastases in PET and metastasis be generated?

The article is divided into five sections. We begin the second section with the methodology, outlining the research technique. We present the results of our analysis, including performance analyses, bibliometric analyses, in Section 3. In Section 4, we present the results, address the research's limitations, and provide recommendations for future studies. In the end, we conclude with our final remarks.

**MATERIAL and METHODS**

Bibliometric analysis was used to examine the literature on PET and metastasis in the context of nuclear medicine. In these analyses, we employed bibliometric techniques such as citation, co-citation, co-occurrence, and co-authorship (27,28). Co-citation is defined as how often two documents are cited together by other documents (29). The more two documents are co-cited, the higher the co-citation strength and the more likely they are to be semantically related. By counting the frequency of occurrence of common words and keywords, disciplinary hotspots can be analysed (30). Co-authorship is a prevalent practice within the field; as such, articles with multiple authors were chosen as an indicator of collaborative activity within the field (31,32).

The Web of Science (WoS) Core Collection, managed by Clarivate, covers seven different databases from 1900 to the present day and provides access to journals from various disciplines. These databases are selected through high quality standards and careful processes. Both Web of Science (WOS) and Scopus have the capability to integrate and organize data in various bibliographic formats for each reference (33,34). In this study, we chose WOS, which contains millions of bibliographic records, billions of citation links and thousands of additional articles. A complete summary of the analysis process is depicted in Figure 1.
On 1.09.2023, publications on "nuclear medicine" AND "PET" AND "metastasis" were searched in the Web of Science (WoS) database, and a total of 588 publications were obtained after applying various extraction strategies. These data were analysed using the R-based, open-source Bibliometrix program (35). First, a performance analysis of these articles was performed, including their basic statistics, authors, number of publications, journals, institutions and countries. Then, a science map was created, including a co-citation network and co-occurrence analysis. The analysis was performed without word aggregation. In the final stage, a list of diseases was created by scanning the abstracts and titles of the articles and counting the recurring disease names one at a time. This final list was categorised according to medical specialities and used to create a new table.

**RESULTS**

In this section, we first analysed the number of publications and citations, the most prolific journals, authors and countries in the field of PET and metastasis through 588 articles. In the second stage, we visualised the PET and metastasis field with co-citation and co-word analyses.

1. **Performance Analysis**

![Figure 2: Main Information](image)

This figure provides an overview of the studies on metastasis using PET scanners in nuclear medicine between 1994 and 2023. First, the time span is quite long, indicating that the topic has long been a focus of interest for the medical and healthcare sectors.

**Main Highlights:** Annual Growth Rate 10.03%: This shows that the topic has received sustained attention and research has increased over the years. Number of Documents 588: A high number of documents may indicate that different aspects of the topic have been covered. Average Number of Citations 27.63: This indicates that studies generally have a high impact. Keywords Plus 1518, Author's Keywords 1241: The number of keywords is quite high, which may indicate that the topic is multi-faceted. Authors and Collaboration Number of Authors 3245: The involvement of a large number of authors may indicate that the topic is of interdisciplinary importance. International Collaborations 24.49%: This suggests that studies are often not limited to one country or region, but are of global importance.
Document Types: Number of Articles 424, Reviews 156: The number of articles is considerably higher than the number of reviews, indicating that first-hand research studies are generally more common. Overall, this dataset shows that the topic of metastasis with PET scanning is an important and constantly evolving area for medical research. The substantial annual growth rate and the average number of citations suggest that these studies are held in high regard by the academic community. The international collaboration rate emphasises the global importance of the topic.

Number of publications and citations by year: The figure shows the number of publications by year (blue bars) and the number of citations by year (red line). Number of Publications by Year: The number of publications has been increasing, especially since the early 2000s. The highest number of publications was reached in 2020. Number of Citations by Year: The data also illustrates a consistent upward trend in the number of citations over time. However, this increase peaked in 2017 and then declined slightly. Overall Assessment: The increase in the number of publications shows that this research area is attracting more and more attention. The peak and subsequent decline in the number of citations may indicate that very influential studies were published during a certain period and then this influence declined slightly. These observations show how research activity and impact have changed over the years. In particular, the increase in the number of publications may indicate that there will be more research in this area in the future. The number of citations, on the other hand, underscores the significance of high-quality studies.

Figure 3: Number of Publications and Citations by Year

Top authors, institutions, journals and countries: Leading Authors: The close number of articles between Fanti S and Bombardieri E indicates that both authors play an important role in nuclear medicine, especially in PET and metastasis. However, it is important to note that although numerically close, there may be qualitative differences depending on the authors’ impact factor and number of citations. On the other hand, authors such as Herrmann K, Eiber M, Kumar R, Mottaghy FM and Rubello D have also made important contributions, although not as much as Fanti S and Bombardieri E regarding the number of articles. Fanti S and Bombardieri E are the most dominant authors in the field with 14 and 13 articles, followed closely by Herrmann K, Eiber M, Kumar R, Mottaghy FM and Rubello D with 10-12 articles, although they are less dominant, and in the lowest ranking, Bal C, Fendler WP and Oyen WJG have made significant contributions to the field with 8 articles.

Leading Academic Institutions: The fact that Udice-French Research Universities leads with 50 papers may indicate the potential of this institution in research and publication quality. The close impact level of the University of Munich and Technical University of Munich indicates that these two German institutions are also important in the field of nuclear medicine. Harvard University, Unicancer and Universite Paris Cite are not as dominant as the top institutions in terms of the number of publications, but they make important contributions. Udice-French Research Universities leads the field with 50 papers, while University of Munich and Technical University of Munich show close impact levels with 38 and 34 papers; Harvard University, Unicancer and Universite Paris Cite are less dominant with 25-29 papers.
Figure 4: Top Authors, Institutions, Journals and Countries

**Leading Journals:** The number of articles between the European Journal of Nuclear Medicine and Molecular Imaging and the Journal of Nuclear Medicine is very close. This may indicate that both journals probably have a high impact factor. Nuclear Medicine Communications and Seminars in Nuclear Medicine may have a similar impact level based on the number of articles. Other journals may have a medium impact. The European Journal of Nuclear Medicine and Molecular Imaging, as well as the Journal of Nuclear Medicine, exhibit comparable and potentially high impact factors, with 41 and 39 articles, respectively. In contrast, Nuclear Medicine Communications and Seminars in Nuclear Medicine have a roughly equivalent number of articles, each totaling 23 and 21, while Clinical Nuclear Medicine and other mid-level journals maintain their impact with 16-14-13 articles.

**Leading Countries:** USA, Germany and Italy are the leading countries in the field of nuclear medicine according to the number of articles. Nonetheless, France, the Netherlands, and the United Kingdom can wield considerable influence, even though they publish fewer papers compared to the top three. Australia, China, and Turkey, despite having a lower publication volume, have secured a place on the list, highlighting their potential for significant contributions in the future. The USA, Germany and Italy lead the way in nuclear medicine research with 375, 340 and 289 papers respectively, while France, the Netherlands and the UK are less influential, with Australia, China and Turkey at the bottom of the list with 72-84 papers.

**Most cited articles:** Table 1 shows the most cited papers on PET (Positron Emission Tomography) and metastasis in nuclear medicine. Citation counts assess the impact of studies with different metrics such as TC per Year and Normalised TC. The relevant metrics are summarised in Table 1.
There are many notable research papers in the field of nuclear medicine, with a particular focus on Positron Emission Tomography (PET) and metastasis. The most cited paper is Rahbar K's 2017 paper in the Journal of Nuclear Medicine, which has received 532 citations. This article addresses the clinical efficacy and safety of 177Lu-PSMA-617 radioligand therapy administered to patients with metastatic castration-resistant prostate cancer (mCRPC) (36). However, when we evaluate it according to the number of citations per year, Rahbar K's paper ranks highest with 76 citations/year. On the other hand, Weber WA's article, which was published in Strahlentherapie und Onkologie in 1999 and received 129 citations in total, has a lower value in terms of annual citations with only 5.16 citations/year. When normalised citation counts are examined, Van Den Wyngaert T's article published in the European Journal of Nuclear Medicine and Molecular Imaging in 2016 is at the top with 7.61. On the other hand, Hoegerle S's article published in the same journal in 2001 ranks the lowest with a normalised citation count of 1.98.

These numerical assessments may not fully reflect the impact and quality of research articles. However, there is not always a correspondence between the annual and normalised number of citations and the total number of citations. For example, although Rahbar K's article is ranked first in the total number of citations, it is not ranked first in the normalised number of citations. The fact that articles published before the 2000s generally have low annual and normalised citation counts may indicate that the impact of these studies may have decreased over time. On the other hand, the fact that articles published in recent years can quickly reach high citation numbers may indicate that these studies address current and effective issues in the field.

In conclusion, this analysis can provide important information about which research studies should be evaluated by which metrics, but it should be kept in mind that these numerical data may not fully reveal the clinical importance or quality of the study.

Rahbar et al's "German Multicenter Study Investigating 177Lu-PSMA-617 Radioligand Therapy in Advanced Prostate Cancer Patients", published in 2017, presents paradigm-shifting findings on metastatic castration-resistant prostate cancer (mCRPC). The study reveals that 177Lu-PSMA-617 radioligand therapy successfully met biochemical response criteria, specifically a 50% reduction in prostate-specific antigen (PSA) levels. This treatment modality, together with positron emission tomography (PET) imaging technologies, is potentially revolutionising the management of metastatic disease. In particular, compared to current third-line systemic therapies, this radioligand therapy guarantees high efficacy and an acceptable safety profile. Thus, this seminal study by Rahbar et al. provides a solid foundation for future oncologic research (36).

Sven N. Reske and Jörg Kotzerke authored "FDG-PET for clinical use: Results of the 3rd German Interdisciplinary Consensus Conference, 'Onko-PET III,' 21 July and 19 September 2000" by Sven N. Reske and Jörg Kotzerke discuss in detail the clinical applications of oncologic positron emission tomography (FDG-PET). The article highlights the capacity of FDG-PET technology to distinguish between benign and malignant lesions, especially in different types of cancer such as lung, pancreatic and lymphoma. It also examines the efficacy of FDG-PET in the post-therapeutic assessment of response to treatment. The article emphasises that FDG-PET applications can play a critical role in optimising treatment processes in cancers managed with radiotherapy and chemotherapy, such as Hodgkin's disease and high-grade non-Hodgkin's lymphoma. In this context, the work of Reske and Kotzerke suggests the potential of FDG-PET imaging in the management of metastatic oncologic pathologies and provides valuable insights into transforming clinical practice regarding this technology (37).
The 2004 study by Selzner et al. examines the comparative effectiveness of contrast-enhanced CT (ceCT) and PET/CT in diagnosing liver metastases in patients with metastatic colorectal cancer. The study, whose primary aim is to demonstrate the direct impact of these imaging modalities on treatment strategies, shows that both modalities have similar sensitivity in identifying intrahepatic metastases. However, it is emphasised that PET/CT is superior to ceCT in identifying intrahepatic recurrence, local recurrence of colorectal origin and extrahepatic metastases, especially in patients with prior hepatotomy. Remarkably, the new findings of PET/CT required a revision of the treatment approach in 21% of the patients studied. This suggests that PET/CT has an important clinical impact in patients with metastatic colorectal cancer, especially in managing liver metastases (38).

The 2017 article by Sundin et al. reviews imaging guidelines for neuroendocrine tumors (NETs) and discusses the benefits and limitations of various modalities in this context. The article underscores that 68Ga-DOTA-somatostatin analog PET/CT is significantly superior for the staging, preoperative imaging, and restaging of Neuroendocrine Tumors (NETs). In particular, this modality is vital in the diagnostic evaluation of lymph node, bone, liver and peritoneal metastases, as well as primary small bowel NETs. In high G2 and G3 NETs, 18FDG-PET/CT is more favorable for prognosis, and these types usually have high glucose metabolism and less somatostatin receptor expression (39).

The 2001 study by Hoegerle et al. examines the efficacy of 18F dopa PET in the diagnostic management of gastrointestinal carcinoid tumors. The study states that this imaging modality is particularly effective in primary tumor and lymph node staging. Overall sensitivity comparisons were 65% for 18F dopa PET, 29% for FDG-PET, 57% for somatostatin-receptor scintigraphy and 73% for morphologic imaging modalities. However, the study emphasises that 18F dopa PET is more effective than other modalities, especially for primary tumor and lymph node localisation. This study suggests that 18F dopa PET can be an effective adjunct in the diagnostic approach of gastrointestinal carcinoid tumors (40).

A study by Lee et al. (41) examined the effectiveness of various techniques for imaging salivary gland tumors. The study particularly emphasises that positron emission tomography (PET) scanning plays a limited role in the evaluation of such tumors. Magnetic resonance imaging (MRI) and computed tomography (CT) are critical for detailed assessment of local invasion, perineural spread and tumor size. Conventional ultrasound techniques are limited in detecting deep tissue extension and malignancy; MRI or CT is mandatory in these conditions. Nuclear medicine modalities and PET scanning often have limited clinical applications. In conclusion, the study confirms that PET scanning is not a primary method for imaging salivary gland tumors and metastasis evaluation.

The study by Chao et al. (42) addresses the rising incidence of radiation necrosis as a result of the increasing use of combination therapies and stereotactic radiosurgery for brain tumors. It was emphasised that standard imaging protocols are insufficient to distinguish between radiation necrosis and tumor recurrence. Sophisticated imaging and nuclear medicine methods also offer a questionable level of accuracy in this regard. The article confirms the efficacy of bevacizumab as a potential treatment for radiation necrosis. However, it does not provide a specific PET scanning and metastasis analysis.

A study conducted by Ohno et al. (43) compared whole-body diffusion-weighted (DW) imaging, whole-body magnetic resonance (MR) imaging and FDG PET/CT used for M-stage assessment in non-small cell lung cancer (NSCLC) patients. Receiver Operator Characteristics (ROC) analysis showed that FDG PET/CT is superior to DW imaging in terms of specificity and accuracy. In particular, full-body MR imaging and DW imaging were found to have similar efficacy to FDG PET/CT. These data emphasise the importance of FDG PET/CT for the accurate evaluation of metastatic spread in NSCLC patients and suggest that MR imaging and DW imaging may be alternative options with high accuracy.

The guidelines approved by the European Association of Nuclear Medicine (EANM) aim to raise the quality standard in nuclear medicine imaging modalities. Specifically, bone scintigraphy is regarded as one of the most sensitive imaging modalities in this field. This technique can assess benign and malignant pathologies as well as physiologic bone turnover processes with high resolution. This study by van den Wyngaert et al. (44) describes in detail how current protocols can be effectively implemented. It also emphasises that bone scintigraphy can be used with high sensitivity, especially for patients with metastatic bone disease. However, it does not exclude the possibility that other nuclear medicine imaging techniques, such as positron emission tomography (PET), may have similar diagnostic capacity.

The study by Calais et al. (45) states that the 68Ga-PSMA-11 PET/CT imaging technique is superior to standard imaging modalities in the detection of early biochemical recurrence (BCR) of prostate cancer, even in patients with serum prostate-specific antigen (PSA) levels below 1 ng/mL. This study analysed how often consensus clinical target volumes (CTVs) in line with Radiation Therapy Oncology Group (RTOG) guidelines cover pathology defined by 68Ga-PSMA-11 PET/CT. The study found that 19 percent of the 270 patients examined, or 52 patients, had PSMA-11 positive lesions that fell outside the consensus CTVs. These findings suggest that it could significantly impact clinical outcomes in salvage radiotherapy (SRT) planning. This could be a remarkable development for the future of PET imaging and metastasis identification, as this modality can be used to more precisely define the anatomical extent of disease, even in its early stages.
Figure 5: Trending Topical Topics

This figure shows a summary of the most common terms used in the literature on PET (Positron Emission Tomography) and metastasis. The frequency and quartile distribution of terms by year reveal which topics are at the forefront of research. For example, terms such as "positron emission tomography" and "18F-fluorodeoxyglucose" indicate the importance of the PET imaging technique and the most commonly used radiopharmaceutical, FDG (Fluorodeoxyglucose). The median years of these terms are quite early (1998 and 2002), indicating that this technology and component has been very active in the literature for a long time.

Regarding metastasis, terms such as "osseous metastases," "skeletal metastases," "lymph-node metastases," and "hepatic metastases" are prominent. These terms illustrate the diversity of research examining how metastases spread to different organs and tissues. In particular, the median year for the term "metastases" is 2016, indicating the timeliness of research on metastasis.

In addition, the median year for the term "guidelines" is 2020, indicating the increasing importance of guidelines and manuals, especially for PET and metastasis. High frequency terms include words such as "management", "diagnosis", and "follow-up". These findings indicate that PET technology is effective not only for diagnostic purposes but also for disease management and follow-up.

In conclusion, the table provides a rich perspective on how PET and metastasis have evolved in the medical imaging and oncology literature. In particular, the emergence of new terms and concepts over time reflects technological and clinical developments in these fields.

**PET (Positron-Emission-Tomography):** Rate of Increase: In 1999 it was mentioned only twice in articles, while in 2023 it was mentioned 204 times. Fastest Increase: A significant increase is observed between 2003-2008. Recent Years: Since 2018, a more stabilised increase is observed. Metastasis (Metastases): Rate of Increase: In 1999, it was mentioned once in articles, whereas it was mentioned 90 times in 2023. Fastest Increase: A rapid increase is observed between 2012-2018. Recent Years: Since 2018, a continuous increase has been observed. FDG-PET: Rate of Increase: In 1999, it was mentioned twice in articles, while in 2023 its frequency increased and it was mentioned 71 times. Other Terms: While the term "Cancer" was mentioned once in articles in 1995, it was mentioned 76 times in 2023. While the term "CT" (Computed Tomography) was mentioned once in 1995, it was mentioned 71 times in 2023.

**Analysis:** The keywords PET and Metastasis have appeared more and more frequently in articles since the 2000s. In recent years, the keyword Metastasis has been mentioned more frequently in articles, even approaching the PET keyword. This may suggest that PET technology is becoming increasingly important in the diagnosis and management of metastasis. FDG-PET appeared more and more frequently in articles from 1999 to 2023, indicating that this modality is gaining importance along with PET. Generic terms such as "cancer" and "CT" also increased in frequency, which may indicate that these topics require a multidisciplinary approach. In conclusion, it is evident that the concepts of PET and metastasis have assumed an increasingly central role in the diagnosis and treatment of cancer, particularly over the past two decades. FDG-PET seems to have an important place in this process.
Bigram Word Cloud Analysis: In this dataset, you will find the frequencies of bigram keywords (combinations of two words) related to PET (positron emission tomography) and metastasis. Below is an analysis of specific keywords and term groups:

PET Related Bigrams
- Positron Emission: 51 times
- Emission Tomography: 35 times
- F--FDG PETCT: 24 times
- FDG PETCT: 14 times
- Emission TomographyComputed: 13 times
- PET Imaging: 13 times
- PETCT Imaging: 13 times

Bigrams Related to Metastasis
- Bone Metastases: 36 times
- Liver Metastases: 21 times
- Lymph Node: 23 times
- Node Metastases: 10 times
- Bone Metastasis: 7 times
- Skeletal Metastases: 9 times

Other Remarkable Bigrams
- Nuclear Medicine: 70 times
- Cancer Patients: 40 times
- Breast Cancer: 48 times
- Prostate Cancer: 97 times
- Thyroid Cancer: 20 times

PET-Based Bigrams: Terms such as "Positron Emission" and "Emission Tomography" frequently appear as key components of PET. FDG-PET is also frequently mentioned. Metastasis-Based Bigrams: Terms such as "Bone Metastases" and "Liver Metastases" indicate that metastasis is frequently investigated, especially in organs such as bone and liver. Cancer Types: Prostate and breast cancer are among the most frequently researched topics. Technology and Methods: Terms such as "Nuclear Medicine" and "Molecular Imaging" underline the importance of imaging techniques. Disease Management: Terms such as "Cancer Patients", "Radical Prostatectomy" indicate that it is related to disease management and treatment strategies. In conclusion, PET and metastasis topics appear in many different contexts in this dataset. In particular, topics such as bone and liver metastases, prostate and breast cancer, as well as specific types of PET such as FDG-PET seem to be very important. The frequent occurrence of terms related to imaging technologies and treatment management shows the importance of a multidisciplinary approach in these fields.

Figure 6: Bigram Word Cloud
2. Scientific Mapping

In this section, co-citation and co-occurrence analyses were performed. Here, the name of each color was determined by using the prominent color clusters and the intellectual structure, conceptual structure and collaboration patterns of the articles on PET and metastasis in nuclear medicine.

2.1. Co-citation Analysis

Co-citation analysis allowed us to visualise the patterns of co-citation between studies in the field and to determine the intensity and strength of the relationships between studies. The authors named the themes after carefully reading the articles collected in each cluster. Based on the results of this co-citation analysis, studies in Cluster 1 address the topics of Positron Emission Tomography (PET) and metastasis within nuclear medicine. Gabriel et al. (1) examined 68Ga-DOTA-Tyr3-octreotide PET compared to somatostatin receptor scintigraphy and CT in neuroendocrine tumors. Adams et al. (2) compared 18 F-FDG PET with conventional imaging modalities in lymph node staging of head and neck cancer. These studies emphasise the role of PET imaging in detecting and monitoring different types of cancers and metastases. Both Gabriel et al. (1) and Adams et al. (2) investigated the advantages and potential limitations of PET imaging over other imaging modes (red cluster). In this context, a suggested theme name for Cluster 1 could be “The Role of PET Imaging in Metastasis and Tumor Staging in Nuclear Medicine”. This theme comprehensively represents the main topics that the cluster focuses on and the diversity of diseases studied.

Cluster 2 studies include research in nuclear medicine, particularly in the detection and evaluation of metastases. For example, Even-Sapir et al. (3) discussed the detection of bone metastases in high-risk prostate cancer patients. Eisenhauer et al. (4) discussed new response assessment criteria in solid tumors. Two studies by Boellaard (5,6) addressed procedural aspects of FDG PET and PET/CT, while Jambor et al. (7) compared different imaging techniques for detecting bone metastases in high-risk breast and prostate cancer patients. Considering the scope of this cluster, we can see that the focus is on metastasis detection and assessment, response criteria and optimisation of imaging protocols. Therefore, a suggested theme name for this cluster is “Nuclear Medicine Applications in Metastasis Detection and Evaluation: Guidelines and Optimisation”. This theme name provides a broad perspective on the main focus of the cluster, which is the detection and management of metastasis, as well as methodological and procedural approaches (blue Cluster).

An appropriate theme name for this Cluster 3 would be “Advancements in PET Imaging for Metastatic Diseases”. The Cluster highlights the role of positron emission tomography (PET) technology in the detection of metastases (especially bone metastases). In particular, there are important studies on various types of cancer (such as breast, prostate and lung cancer) and the role of this technology. The 1998 study by Cook et al. examined how effective 18FDG PET technology is for detecting bone metastases in breast cancer patients. Particular emphasis is placed on the different metabolic activities between osteoblastic and osteolytic lesions (8). Hamaoka's 2004 article provides a comprehensive overview of metastatic breast cancer bone imaging. It evaluates the effectiveness of different imaging techniques as well as PET in particular (9). The 1996 article by Shreve et al. examines the effectiveness of PET and 2-deoxy-2-[F-18] fluoro-D-glucose (FDG) in the diagnosis of metastatic prostate cancer. This suggests that PET may have a potential role in breast cancer and other types of cancer such as prostate cancer (10). In 2013, Damle et al. provide a comparative study of the role of 18 F-fluoride PET-CT in detecting bone metastases in breast, lung and prostate cancer patients. This study provides a broader perspective by combining PET applications in different cancer types (11). In 2003, Gallowitsch and colleagues present a study comparing F-18 fluorodeoxyglucose PET with conventional imaging modalities in the follow-up of breast cancer patients. This is another important data point to show how effective PET is in detecting recurrent or metastatic disease (12). From this detailed perspective, it can be said that the theme “Advancements in PET Imaging for Metastatic Diseases” broadly covers the critical issues that the studies in this cluster focus on (green cluster).

Clinical and Methodological Efficacy of PSMA Liganded PET/CT Imaging in Prostate Cancer Diagnosis" Sensitivity and Specificity of PSMA Liganded PET Imaging: This sub-theme addresses the sensitivity and specificity of PSMA ligand PET imaging in the diagnosis of prostate cancer. Hofman et al. (46) extensively investigated the sensitivity and specificity of such imaging in prostate cancer diagnosis. Similarly, Perera et al. (47) and Maurer et al. (48) have also examined the sensitivity and specificity of this type of imaging through systematic reviews and meta-analyses. These studies emphasise the superiority of PSMA liganded PET imaging over conventional methods in the diagnosis of prostate cancer. Standardisation of PSMA-Liganded PET/CT Imaging: This sub-theme focuses on standardisation and unification of imaging. Eiber et al. (49) presented the proposed miTNM classification for the evaluation of PET/CT with PSMA ligand. Fendler et al. (50) introduced procedural pathways endorsed by the European Association of Nuclear Medicine (EANM) and the Society for Nuclear Medicine and Molecular Imaging of America (SNMNI). These studies make important contributions to the establishment of methodological standards. These themes provide a comprehensive understanding of the clinical and methodological effectiveness of PSMA ligand PET/CT imaging in prostate cancer diagnosis. Sensitivity and specificity issues emphasise the effectiveness of the method in terms of clinical outcomes. On the other hand, standardisation efforts allow for general acceptance of this imaging technique and unification of applications (Purple cluster).

Orange Cluster (single author): "PET and SPECT Imaging Comparisons of Neuroendocrine Tumors with Gallium-68 and Indium-111 Markers": This article compares the efficacy of DOTATOC PET imaging using the Gallium-68 (Ga-68) marker and DTPAOC (Octreoscan) SPECT imaging using the Indium-111 (In-111) marker in the diagnosis of neuroendocrine tumors (51). Bibliometric parameters such as citations, betweenness, closeness and PageRank show the impact and importance of this
article in the field. The article provides important information on the comparison of two different radioactive markers and imaging techniques used in the diagnosis of neuroendocrine tumors.

Figure 7: Co citation network analysis

2.2. Co-occurrence Analysis:

The results of this co-occurrence network analysis aim to review the literature in nuclear medicine, specifically on PET imaging techniques and the detection and evaluation of metastasis. We propose the following theme names for each cluster: Cluster 1: "PET and Cancer Types": This cluster includes topics such as positron-emission tomography (PET), metastases, carcinomas, diagnosis and follow-up. The word "positron-emission-tomography" determines the most important theme of this cluster as it has the highest Betweenness, Closeness and PageRank values. That is, PET imaging is the most central and connected topic. Words such as "metastases" and "carcinoma" also hold significant importance, although not as central as "PET." Cluster 2: "FDG-PET and Radiotherapy": This cluster covers topics such as FDG-PET, computed tomography, lymph node metastases. "FDG-PET" is the main theme of this cluster with high Betweenness and PageRank values. However, "computed-tomography" also has a high interaction and is closely related to FDG-PET. Cluster 3: "Prostate Cancer and Recurrence": This small cluster includes terms related to prostate cancer, such as radical prostatectomy and biochemical recurrence. The word "radical prostatectomy" is the main theme of this cluster with the highest Betweenness and PageRank values. Cluster 4: "Cancer Management and Imaging": This cluster covers various topics such as cancer management, CT, impact, liver metastases. "CT" and "management" are this cluster's two most important themes with high Betweenness and PageRank values. When determining the importance of words for each cluster, it is useful to consider Betweenness, Closeness and PageRank values. For example, a word with a high Betweenness value may have a more central role in linking that theme to other themes. Similarly, a high PageRank value indicates how important a word is in that theme.

Figure 8: Co Occurrence Network Analysis
2.3 Co-Author Analysis:

When we review the studies, we will examine in detail the topics on which the most frequent co-author pairs focused. For example, Kumar R and Sharma P were specifically associated with keywords such as "Bone Scintigraphy," "Conventional Imaging," "Metastases," and "Sensitivity." Kumar R and Bal C were also associated with similar keywords, indicating that they focused on Skeletal metastasis and other topics. The author pair of Bal C and Sharma P also focused on topics such as "Bone Scintigraphy," "Metastases" and "Susceptibility," indicating an important focus in this field.

The pair of Bombardieri E and Crippa F, on the other hand, point to a different area with keywords such as "Breast Cancer," "Radionuclide Imaging" and "Treatment Outcome." Fanti S and Farolfi A, especially on "Metastatic castration-resistant prostate cancer" and Lutetium; Kumar R and Karunanithi S, on Bone Scintigraphy and F-18. Catalano OA and Soricelli A studied "Breast Cancer" and "Colorectal Cancer" using Diffusion-Weighted Imaging and FDG-PET/CT techniques. The pair of Soricelli A and Salvatore M share similar topics and keywords with the pair of Catalano OA and Salvatore M. This suggests that the authors addressed the same topics from different perspectives.

Finally, the pair of Robin P and Salaun PY focused on highly specific and niche topics, such as "Adrenocortical Adenoma," such as "Bone Metastasis" and "Medullary Thyroid Carcinoma". This diversity suggests that author pairs are engaged in various subtopics and keywords, contributing to a more comprehensive and well-rounded understanding of the overall field. This analysis provides insight into which topics the authors are focusing on and which areas of research they could potentially collaborate more on. For example, Kumar R and Sharma P appear to be working on the same topics, indicating a high potential for collaboration. These comments further elaborate on the topics the authors are working on together and the potential for collaboration on these topics.

Figure 9: Collaboration Network Analysis

DISCUSSION

PET scans are of great interest in the field of medical imaging due to their important role in the early detection and management of metastases. In this chapter, we will explore the role of PET scans in this field and how different perspectives have been addressed. From the perspective of the importance of PET scans in metastasis detection, PET scans in cancer diagnosis are recognised as a critical tool, especially in the detection of metastases. The importance of such scans has been emphasised in studies by Gabriel et al. (1) and Adams et al. (2). These studies clearly show that PET imaging is effective in the detection of metastatic diseases. Studies such as Cook et al. (8), Hamaoka et al. (9), Shreve et al. (10), Damle et al. (11) and Gallowitsch et al. (12) also support the usefulness of PET scans in the early detection of cancer metastases.

In terms of Comparison of Different Imaging Techniques, this study also addresses the importance of the diagnostic performance of different imaging techniques. Studies such as Cebeci et al. (18), Dellepiane et al. (19) and Zadeh (20) show that PET scans have high efficacy in the diagnosis of specific cancer types, especially prostate cancer and bone metastases. In terms of Patient Management and Follow-up, the management and follow-up of metastases is important for patient prognosis and quality of life. In this context, it has been emphasised that PET scans can play a critical role in early detection of metastases and monitoring treatment response (21,22). In the context of health policy and economic issues, it is important to address issues such as cost-effectiveness and accessibility of PET scans. This study did not assess the economic impact of PET scans on...
cancer diagnosis and management, and this may need to be considered as an area for future research. Regarding Education and Awareness, it is crucial to emphasize the significance of fostering knowledge and awareness about PET scans and the risk of metastasis among both healthcare professionals and the general public. This is a critical step for early detection and effective intervention. In conclusion, there exists a rich body of research within the field of nuclear medicine that aids in our deeper comprehension of the significance of PET scans in the diagnosis of metastases and the dynamic interplay between these two concepts. However, the findings of these studies need to be considered in conjunction with different research studies, clinical applications and policy discussions.

**Evaluation in terms of Co-Citation:** Red Cluster (Cluster 1): This cluster focuses on the role of PET imaging in metastasis and tumor staging in nuclear medicine. Studies such as Gabriel et al. (1) and Adams et al. (2) have addressed the effectiveness of PET imaging in detecting different types of cancers and its advantages over other imaging modes. Blue Cluster (Cluster 2): This cluster offers a broader metastasis detection and evaluation perspective. Studies such as Even-Sapir et al. (3) and Eisenhauer et al. (4) provide a more comprehensive view, including methodological and procedural approaches as well as disease detection and management. Green Cluster (Cluster 3): This cluster focuses on the role of PET imaging in metastatic disease. Studies such as Cook et al. (8), Hamaoka et al. (9) and Damle et al. (11) deepen the understanding of this topic by addressing the effectiveness of PET in different cancer types. Purple Cluster: This cluster focuses on the clinical and methodological efficacy of PET/CT imaging with PSMA ligand in prostate cancer. Studies such as Hofman et al. (46), Perera et al. (47) and Maurer et al. (48) address the sensitivity and specificity of this type of imaging, while Eiber et al. (49) and Fendler et al. (50) work on standardisation. Orange Cluster (single author): This cluster compares PET and SPECT imaging using Gallium-68 and Indium-111 markers (51). This paper provides important insights into the diagnosis of neuroendocrine tumors by comparing the effectiveness of two different radioactive markers and imaging techniques.

Clusters need to be positioned according to different cancer types and technologies. The red and green clusters address the effectiveness of PET in different cancer types, while the purple cluster focuses specifically on prostate cancer. The blue and purple clusters present studies on standardisation and optimisation of imaging techniques. The purple cluster shows a strong focus on sensitivity and specificity of imaging techniques. The orange cluster reveals differences between two different markers and imaging techniques, a feature not seen in the other clusters. This analysis provides a comprehensive understanding of each cluster's main issues and differences. This can be useful to guide future research.

The results of the co-occurrence network analysis reveal important theme clusters of relevant literature on PET imaging techniques and metastasis detection and evaluation in nuclear medicine. The first cluster of themes is named "PET and Cancer Types" and includes topics such as cancer types, metastases, carcinomas, etc. in PET imaging. Within this theme, "Positron-emission-tomography" stands out as the most central and relevant topic. The second cluster of themes is called "FDG-PET and Radiotherapy" and includes topics such as FDG-PET, computed tomography, lymph node metastases. The third cluster of themes is named "Prostate Cancer and Recurrence" and includes terms associated with prostate cancer such as radical prostatectomy and biochemical recurrence. The fourth and final cluster of themes is called "Cancer Management and Imaging" and covers topics such as cancer management, CT, liver metastases. These themes reflect the different focal points of research in nuclear medicine.

The results of the bigram analysis support these themes in more detail. "PET-Related Bigrams" emphasise the key components of PET, especially with terms such as "Positron Emission" and "Emission Tomography". "Metastasis-Based Bigrams" show that bone and liver metastases are research foci. "Prostate Cancer" and "Breast Cancer" stand out among the bigrams supporting the "Types of Cancer" theme. Bigrams related to "Technology and Methods" emphasise the importance of imaging techniques. Bigrams related to "Disease Management" focus on disease management and treatment strategies.

These analyses highlight various aspects of PET imaging techniques and metastasis in nuclear medicine. In particular, it shows the importance of themes such as cancer types, technology and imaging modalities, disease management and treatment strategies in this field. These findings emphasise the diverse focus of nuclear medicine research and the need for a multidisciplinary approach.

**CONCLUSION**

Our bibliometric investigation underscores the pivotal role of PET imaging modalities in delineating and clinically managing metastatic disease. The analysis unequivocally establishes the diagnostic acumen of PET scans in oncologic settings, underlining their superiority in detecting metastatic foci and ensuring accurate staging. This aids in tailoring therapeutic interventions, optimising patient outcomes, and monitoring disease progression or regression. Nonetheless, while the clinical potential of PET imaging is evident, there is an emergent need to address considerations related to its cost-effectiveness and broader accessibility within healthcare systems. Additionally, enhancing the dissemination of knowledge regarding its capabilities and applications becomes paramount for clinicians and stakeholders alike. In summary, the advancements in PET-based nuclear medicine not only represent the current pinnacle of diagnostic radiology but also provide a promising path for future scholarly endeavors and clinical innovations.

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