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FEASIBILITY OF [64CU]CU-TRASTUZUMAB PET/CT IMAGING IN BREAST CANCER: A SYSTEMATIC REVIEW

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Abstract

Purpose: [^{64}Cu]Cu-NOTA/DOTA-trastuzumab PET/CT imaging can non-invasively identify human epidermal growth factor receptor 2 (HER2)-positive breast cancer (BC). In addition to presenting literature-based evidence for dosimetry and pharmacologic safety of [^{64}Cu]Cu- NOTA/DOTA-trastuzumab in patients, this systematic review aims to demonstrate the viability of [^{64}Cu]Cu-trastuzumab PET/CT in identifying and assessing trastuzumab tumor uptake in people with HER2-positive metastatic BC.

Methods: We searched the PubMed, Scopus, and EMBASE databases to find pertinent English-language papers concerning [^{64}Cu]Cu- NOTA/DOTA-trastuzumab PET/CT for BC diagnosis. Other items were also manually searched.

Conclusion: The feasibility of [^{64}Cu]Cu -trastuzumab PET/CT for the identification of HER2-positive lesions was reviewed. [^{64}Cu]Cu-DOTA/NOTA-trastuzumab reveals HER2-positive metastatic BC with high sensitivity and is effective in surveying distributed disease. Moreover, [^{64}Cu] Cu-labeled trastuzumab may possibly be applied to decide on the right patients and right timing for HER2 therapy, to observe the treatment response after HER2-targeted therapy, and not only for the detection of primary HER2-positive BC but also for metastatic HER2-positive lesions. The advancement of [64Cu]Cu-trastuzumab PET/CT for the detection of BC is encouraging. However, more studies are required to determine the usefulness rate of imaging plans for clinical administrations.

Keywords: [^{64}Cu]Cu-trastuzumab; PET/CT; Breast Cancer, and HER2

Introduction

Trastuzumab is a targeted cancer drug. It is a treatment for early and advanced breast cancer (BC), and advanced stomach cancer [1]. It is a man-made antibody that targets the extracellular portion of HER2 and is the primary HER2-targeted agent acknowledged by the U.S. FDA for taking care of both primary and metastatic HER2-overexpressing BC [2]. Protein overexpression or gene amplification or both, is the way of determining HER2 positivity and is found in 25–30% of BCs [2]. Trastuzumab-based HER2 imaging has received rising interest. Studies have shown that [^{64}Cu]Cu-NOTA and DOTA-trastuzumab PET have paramount importance for the detection of HER2-positive lesions in patients with early-stage and metastatic BC [3, 4].

HER2 is a central target in the management of BC. Therefore, the assessment of HER2 is vital step in the diagnostic areas and the selection of optimal treatments in both early-stage and metastatic settings[5, 6].

HER2-positive Trastuzumab, a humanized monoclonal antibody that targets HER2, is frequently used to treat BC. Numerous efforts have been made to noninvasively evaluate the expression of HER2 using radioisotopes. In the beginning, single photon emission computed tomography (SPECT), a technique for non-invasive imaging was used to perform HER2 imaging [7, 8]. In a clinical study, it was demonstrated that Indium-111 (^{111}In) classified trastuzumab ability to detect metastatic lesions that are HER2-positive [8]. This study suggests that SPECT may be valuable as a clinical diagnostic instrument even though it has drawbacks like poor spatial resolution or low sensitivity for the tissues at depth.

To overwhelm these limitations, Iodine-124 (^{124}I) and Zirconium-89 (^{89}Zr) labeled antibodies were evaluated in HER2-positive BC [9-11]. [^{89}Zr]Zr-trastuzumab patients with metastatic HER2-positive BC participated in a PET trial [12]. In HER2-positive lesions, the study found that PET improved visibility and semi-quantitative uptake [12].

Unfortunately, ^{111}In, ^{124}I, and ^{89}Zr radiolabeled trastuzumab resulted in high radiation exposure in patients, due to their long half-lives[13]. Because of the radioisotope's shorter half-life, [64Cu]Cu-NOTA-trastuzumab PET may be able to produce good contrast with high resolution and less exposure (12.7 h) [14].

Therefore, it is a good time to conduct a systematic review with major attention to the basic principles of [^{64}Cu] Cu-trastuzumab using NOTA and DOTA as chelators and its potential use in BC diagnostics via PET/CT imaging. This systematic review summarizes the physical and methodological concept of [^{64}Cu] Cu-NOTA/DOTA-trastuzumab in PET/CT imaging for identification of breast cancer.

Materials and Methods

This systematic review was written using a pre-defined protocol to review the principle and potential of [64Cu] Cu-trastuzumab in the assessment of BC. In the presentation of the study's report, the recommended reporting items for systematic reviews and meta-analyses were adhered to (PRISMA) [15].

Literature Search

Relevant published articles about [^{64}Cu] Cu-NOTA/DOTA-trastuzumab PET imaging were identified. PubMed, EMBASE, and Scopus databases were used to search for relevant articles. A principal plan was settled in PubMed and then interpreted for each database. Controlled vocabulary and keyword terms were used for all search strategies to define the concepts of [^{64}Cu] Cu-trastuzumab PET imaging. For keywords, the following search process was employed : ("[^{64}Cu] Cu-Trastuzumab"[tiab] OR "[^{64}Cu] Cu-NOTA-trastuzumab"[tiab]) OR “[^{64}Cu] Cu-DOTA-trastuzumab”[tiab] OR “Copper-64 trastuzumab” [tiab] AND ("positron emission tomography"[tiab]

OR "PET"[tiab]) AND ("breast cancer"[tiab] OR ("human epidermal growth factor receptor 2"[tiab] OR "HER2"[tiab])). Additionally, manually searched articles using references from saved articles were included. The searches were done on May 30th, 2022. After the search was completed duplications were eliminated. After then, Endnote (version X8, for Windows operating system, Thomson Reuters, Philadelphia, PA, USA) was used to download the articles. to preserve and achieve the citation review process.

Inclusion Criteria

This systematic review included all available articles that evaluated the principle and potential of [^{64}Cu] Cu-trastuzumab PET imaging was engaged. The encompassed articles should have met the following inclusion criteria's: (a) Evaluating [^{64}Cu]Cu-trastuzumab PET imaging; (b) Imaging only for detection of breast cancer; (c) both clinical and pre-clinical studies were included; (d) Research that almost comprehensive or arises recent selections, duplications were eliminated.

Exclusion criteria

The following criteria were used to exclude some articles: (a) non-PET studies; (b) case studies, reviews, conferences, dings, letters, and reviews; (c) studies of languages other than English.

Data extraction

Two independent reviewers examined all downloaded articles based on the inclusion and exclusion criteria for their eligibility and discrepancies were resolved through discussion with a third author. If the abstract passed the criteria, a whole article evaluation was done. Then, the whole article of appropriate studies saved was reserved for review.

We took the following information out of each eligible article: the names of the authors, the publication year, the country where the study was done, how many patients were involved, their ages, the type of medication they were taking, and how long they had trastuzumab imaging.

3. Result

Literature search

The summary of search results is presented in Figure 1. For the initial search, we discovered 50 records altogether, PubMed (20), Scopus (16), Embase (10), and, 4 hand searching. Of the 50 records, 20 were retained after removing duplication. 12 articles were excluded after testing their abstract and full text based on the criteria for inclusion and exemption.

Reasons for the exclusion: articles not [^{64}Cu] Cu-trastuzumab (n=4); besides those concerned with Neuroendocrine Tumors (n=6) and case reports (2). Finally, a total of 8 articles [3, 4, 13, 16-20] were included in this study. Detailed information on all eligible studies is provided in Table 1.

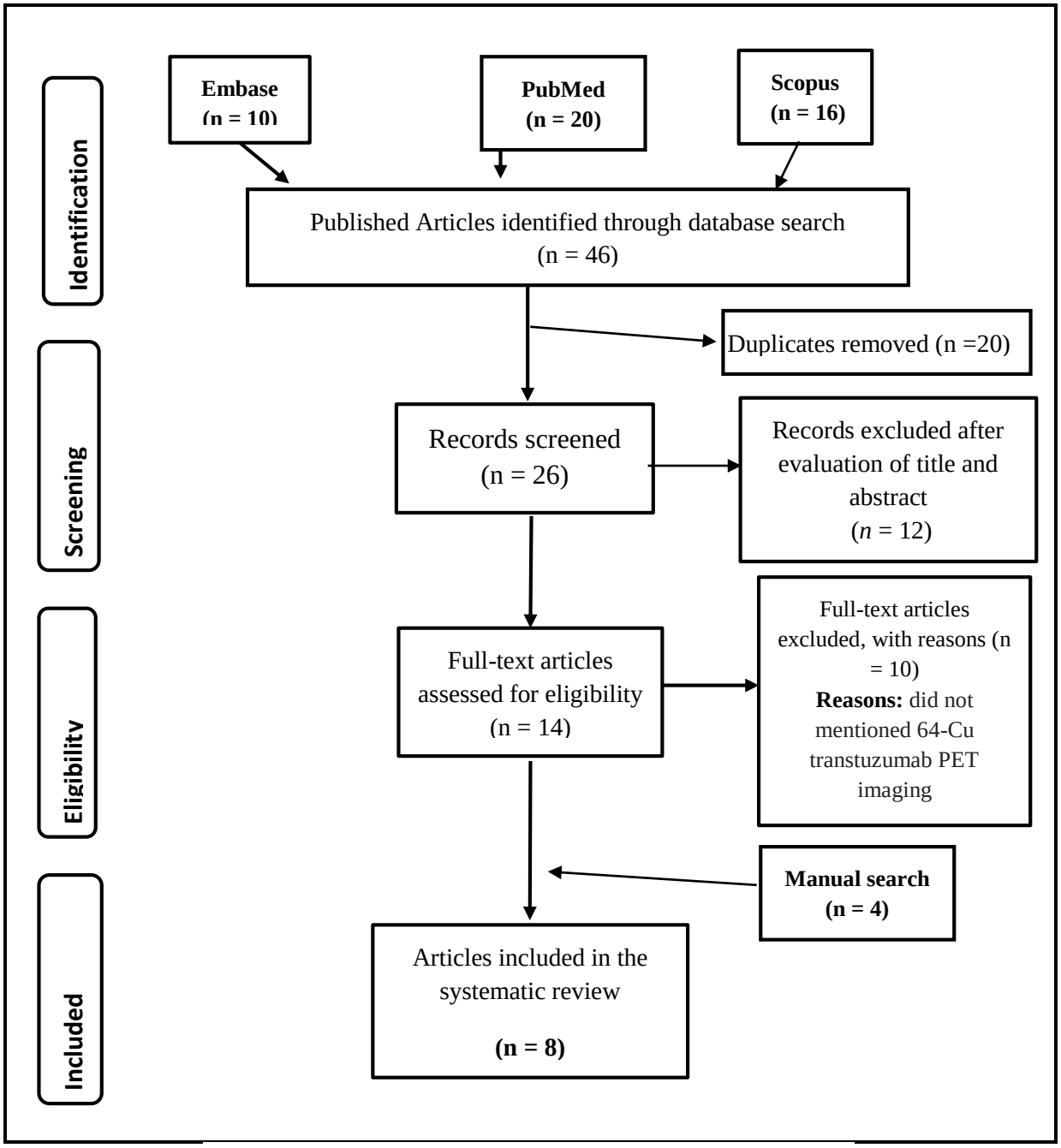

Figure 1. PRISMA flow diagram for the systematic review

Author	Year	Location	No. of patients	Age	Name of the drug	Dose of the drug	Optimal timing for image
Mortimer *et al [17]*	2013	California, USA	8	56 (39-75)	64Cu-DOTA-trastuzumab	364–512 MBq, 5 mg of trastuzumab	21–25 (day 1) and 47–49 (day 2) h after injection
Tamura *et al [11]*	2013	Japan	6	median age of 58 years	64Cu-DOTA-trastuzumab	130MBq	1, 24, and 48 h after injection
Carrasquillo *et al [14]*	2016	New York, USA	11	median age of 52; range of 31-61	64Cu-trastuzumab	296-370 MBq/5 mg	Immediately post-injection and at 24 hours post-injection.
Lee *et al [16]*	2021	Korea	7	40–80 years	64Cu-NOTA-Trastuzumab	296 MBq	1, 24, and 48 h after injection
Woo *et al [20]*	2019	Korea	-	-	^{64}Cu-NOTA-trastuzumab	7.4 MBq	24 h after injection

Mortimer *et al [18]*	2017	California, USA	18	59 y (age range, 35–75 y)	64Cu-DOTA-trastuzumab	364–551 MBq, 5 mg of trastuzumab	21–25 (day 1) and 47–49 (day 2) h after injection
Kurihara *et al [15]*	2015	Japan	5	20 - 75 years.	^{64}Cu-DOTA-trastuzumab	130 MBq	24 or 48 h after the injection
Sasada *et al [19]*	2017	Japan	38	52	64Cu-DOTA-trastuzumab	-	48 h after the injection

Table 1. Summary of studies describing the feasibility of [^{64}Cu]Cu-trastuzumab PET/CT breast cancer imaging

3.1. Production of Copper Radionuclides

Table 2 shows the decay characteristics of copper radioisotopes[21]. Copper (Z = 29) has two table isotopes, ^{63}Cu (69.15%) and ^{65}Cu (30.85%), and 27 radioisotopes. Among them, there are four positron emitters, ^{60}Cu ($T_{1/2}$ = 23.7 min, 93% β^+), ^{61}Cu ($T_{1/2}$ = 3.33 h, 61% β^+), ^{62}Cu ($T_{1/2}$ = 9.7 min, 98% β^+) and ^{64}Cu ($T_{1/2}$ = 12.7 h, 19%β^+, 38% β^-), and an electron emitter, ^{67}Cu ($T_{1/2}$ = 61.83 h, 100% β^-). Cu-64 possesses unique decay characteristics that make it a multipurpose radionuclide with many potential applications. It decays with a half-life of 12.7 h via three modes: positron emission (17.5% β^+), beta emission (38.5% β^-) and electron capture (44.0% EC)

Table 2: The decay characteristics of copper radioisotopes

Isotope	$T_{1/2}$	β^- MeV (%)	β^+ MeV (%)	EC (%)	γ MeV (%)
^{60}Cu	23.4 minutes	—	2.00 (69) 3.00 (18) 3.92 (6)	7.0	0.511 (186) 0.85 (15) 1.33 (80) 1.76 (52) 2.13 (6)
^{61}Cu	3.32 hours	—	1.22 (60%)	40	0.284 (12) 0.38 (3) 0.511 (120)
^{62}Cu	9.76 minutes	—	2.91 (97%)	2	0.511 (194)
^{64}Cu	12.7 hours	0.573 (38.4)	0.655 (17.8%)	43.8	0.511 (35.6) 1.35 (0.6)
^{67}Cu	62.0 hours	0.395 (45) 0.484 (35) 0.577 (20)	—	—	0.184 (40)

McCarthy et al. have reported the effective fabrication way of high-specific activity ^{64}Cu by using a small biomedical cyclotron and ^{64}Ni-enriched (> 95%) [23]. ^{64}Ni (p, n)^{64}Cu transmutation reaction is high yield (2.3–5.0 mCi h^{-1}), however, it can be optimized to 95–310 mCiμg^{-1} after being purified with an ion-exchange column. Obata et al., defined yields of more than three mCi/μAh, using a 12Mev cyclotron with high purity radionuclide [25], Moreover, Avila-Rodriguez et al. enhanced yields to >7 mCi/μAh with 11.4-MeV protons [28]. Finally, Szajek et al., enhance yields to 10.5 ± 3 mCi/μAh when irradiated with a 12.5-MeV proton beam, [29]. Currently, the use of copper-64 isotope is radically increased [30] and its fabrication has been reported by academic affairs in the US [26, 27], EU [25], and Japan [21].

3.2 Human epidermal growth factor receptor-2 (HER2)

The human epidermal growth factor receptor-2 (HER2; also known as c-erbB-2 or HER2/neu) is one of the most promising of molecular marker that has been identified that may has prognostic value. HER2 also known as ERBB2, is a protein that plays a crucial role in cell growth and division. It is a member of the epidermal growth factor receptor (EGFR) family of proteins [31]. HER2 is often associated with certain types of cancers, particularly breast cancer, where it can have significant clinical implications. HER2 is known by its overexpression in certain cancers. The overexpression of HER—an intrinsic protein tyrosine kinase—is strictly connected to rapid-progress tumours [32]. HER2/neu (HER2) a member of the HER receptor family is most commonly associated with breast

cancer, it can also be overexpressed in other types of cancer, such as gastric cancer and some types of lung cancer [18]
The HER2 protein is a 185-kD transmembrane glycoprotein and a member of the HER family of growth factor receptors [33]. HER2 heterodimerizes with other members of the HER family and participates in signal transduction cascades [34]. HER2 is frequently associated with breast cancer. Approximately 15-20% of breast cancers exhibit HER2 overexpression or amplification. This type of breast cancer is often referred to as HER2-positive breast cancer. HER2 overexpression has been detected in 20 to 30% of human breast carcinomas and studies have indicated that HER2 overexpression plays a role in malignant transformation and tumorigenesis [35] as presented the first report on HER2 gene amplification in ductal carcinoma in situ (DCIS) breast cancer by and was associated with the comedo carcinoma variant.

HER2 status is an important prognostic factor in breast cancer. HER2-positive breast cancers tend to be more aggressive and have a higher risk of recurrence compared to HER2-negative breast cancers. Sylvie Ménard et al [31] studied the relationship between HER2 positivity and morphological and biological alterations and how they impact on prognosis in breast cancer and the results revealed that in node-negative patients, the prognostic value of HER2 remains controversial. A large, retrospective analysis confirmed that HER2 independently predicts poor prognosis in node-positive breast cancer patients. The study also indicated that Evaluation of HER2 status in combination with other prognostic markers enhances the accuracy and power of the predictive prognosis and should help to more clearly define the most appropriate treatment for the individual patient.

HER2 status is determined through various diagnostic tests, including immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH). These tests help determine whether HER2 is overexpressed or amplified in a patient's tumor tissue. HER2 status is determined through various diagnostic tests, including immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH). These tests help determine whether HER2 is overexpressed or amplified in a patient's tumor tissue.

3.3. [^{64}Cu]Cu-NOTA-Trastuzumab PET/CT Imaging of HER2

Research has revealed that [^{64}Cu] Cu-NOTA-trastuzumab PET has paramount importance in finding HER2-positive tumours in those who have both primary and metastatic BC [2-12]. To manage BC, HER2 is an important target. As a result, HER2 evaluation is an essential step in the diagnosis and choice of the best therapy in both early-stage and metastatic contexts. HER2 imaging using [^{64}Cu]Cu-trastuzumab has getting more attention of the researchers. HER2 is a verified therapeutic target in the breast and gastric cancer, and over expressed in several cancers, including breast, gastric, ovary, prostate, bladder, and lung cancers [5, 6]. 15%–25% of BC patients have HER2 overexpression, which is typically associated with a clinically devastating course. Clear classification and the use of a variety of anti-HER2 medications have significantly improved patient outcomes in both advanced and early illness situations [36].

3.3.1. Pre-clinical studies

According to preclinical research, [^{64}Cu]Cu-NOTA-trastuzumab successfully targeted the HER2-expressing tumor in vitro and showed a comparatively low absorbed dose because of a brief residence period [4, 37-39]. Sang-Keun Woo et al [4] did a study on HER2-positive BC xenograft biodistribution and small-animal PET imaging (BT-474). The internal dosimetry for test animals was determined using the Monte Carlo N-particle algorithm. According to the report of the study, there was no difference observed regarding biodistribution data of [^{64}Cu]Cu-NOTA-trastuzumab uptake between the main tissues and organs in mice with and without tumors. Even though slowly decreased over time, at two hours, there was a lot of radioactivity in the spleen and blood [4]. Moreover, the results revealed that the calculated absorbed dose of [^{64}Cu]Cu-DOTA-trastuzumab in the heart, liver, and spleen is greater than that of [^{64}Cu]Cu-NOTA-trastuzumab due to a brief dwell time and

[^{64}Cu]Cu-NOTA-trastuzumab was successfully directed, both in vivo and in vitro, at the HER2-expressing malignancies. The research concluded by summarizing that in human studies, the appropriate timing for patient selection for HER2 treatment and for tracking the outcome of HER2-targeted treatment, [^{64}Cu]Cu-NOTA-trastuzumab has paramount importance [4]

3.3.2. Clinical studies

Carrasquillo et al [16] conducted research on the reliability, practicality, safety, and pharmacokinetics of PET imaging using [^{64}Cu]Cu-trastuzumab. Their findings revealed that, patients experienced no significant adverse problems and [^{64}Cu]Cu-trastuzumab PET imaging was feasible, safe, and reproducible.

Another interesting study was performed by Inki Lee et al [18] to evaluate both the biodistribution and safety of [^{64}Cu]Cu-NOTA-trastuzumab, a novel ^{64}Cu-labeled PET tracer for HER2 in patients with BC. The study was done on seven patients with BC and PET images were taken at 1, 24, and 48 h after 296 MBq of [^{64}Cu] Cu-NOTA-trastuzumab injection. The finding of the study revealed that [^{64}Cu]Cu-NOTA-trastuzumab PET images revealed that the overall mean standard uptake (SUVmean) values in each organ negatively associated with time. After 48 h administration, the SUVmax of HER2-positive tumors was relatively higher than HER2-negative tumors. HER2-positive tumors showed higher tumor-to-background ratios than in the HHER2-negative tumors. Furthermore, The calculated effective dose by the OLINDA/EXM software with a 296 MBq injection of [^{64}Cu]Cu-NOTA-trastuzumab was 2.96 mSv. The highest absorbed dose was observed in the liver followed by the spleen and heart wall. Regarding safety, no contrary events related to the use of [^{64}Cu]Cu-NOTA-trastuzumab were reported.

3.4. [^{64}Cu]Cu-DOTA-Trastuzumab PET/CT Imaging of HER2

Interestingly, Tamura K. et al [13] revealed for the first time in people the safety, distribution, internal dosimetry, and early HER2-positive tumor pictures of [^{64}Cu]Cu-DOTA-trastuzumab. Six patients with main or metastatic HER2-positive BC underwent the test at 1, 24, and 48 hours after receiving an administration of about 130 MBq of the probe [^{64}Cu]Cu-DOTA-trastuzumab. Data were collected from blood, urine, and normal tissue, and the probe's internal dosimetry and multiorgan biodistribution were assessed. After the administration of [^{64}Cu]Cu-DOTA-trastuzumab safety data were gathered for all the patients and during the 1-week follow-up period. The results showed that although [^{64}Cu]Cu-DOTA-trastuzumab absorption in normal tissues was low, blood radioactivity was high and radiation exposure during [^{64}Cu]Cu-DOTA-trastuzumab PET was equivalent to that during traditional [^{18}F]FDG-PET. The study's findings also showed that the dosimetry and pharmacologic safety outcomes were satisfactory at the dose required for adequate PET imaging [13].

Another study directed by Sasada et al[20] showed the [^{64}Cu]Cu-DOTA-trastuzumab PET/CT imaging of 38 patients for assessment of HER2 status strongly correlated with histologic HER2 expression status. When compared to the conventional way of determining the HER2 status of tumor tissue, HER2-PET imaging has the potential to be a non-invasive alternative. Brain metastases could be also detected using [^{64}Cu]Cu-DOTA-trastuzumab PET imaging from HER2-positive BC [17].

Mortimer G.E et al [19] conducted research to examine the PET/CT of [^{64}Cu]Cu-DOTA-trastuzumab for determining the tumour uptake of trastuzumab in patients with metastatic BC that was HER2-positive. For this purpose, eight women with selection criteria of biopsy-confirmed HER2-positive metastatic BC and no anti-HER2 therapy for 4 months or longer were selected to undergo complete staging, including [^{18}F]FDG PET/CT [19]. The procedures they used for imaging were as follows: For six of the eight patients, [^{64}Cu]Cu-DOTA-trastuzumab injection (364–512 MBq, 5 mg of trastuzumab) was headed by trastuzumab infusion (45 mg). PET/CT (PET scan duration 1 h) was performed 21–25 minutes (day 1) and 47–49 minutes (day 2) h after [^{64}Cu]Cu-DOTA-trastuzumab injection. Based on the [^{18}F]FDG PET/CT scan fields of view were chosen. Only lesions remarkable

on CT were used to determine tumor detection sensitivity and uptake analyses; lesions envisioned relatively to adjacent tissue on PET were considered PET positive. Maximum single-voxel standardized uptake value (SUVmax) was used to measure uptake in prominent lesions. The study's findings showed that the 45-mg trastuzumab predose reduced liver absorption of ^{64}Cu by around 75% without significantly impacting tumor uptake. The examination included 89 CT-positive lesions. On average, there was no difference observed regarding tumor uptake between [^{64}Cu]Cu-DOTA-trastuzumab and ^{18}F-FDG, but SUVmax was not interrelated between the two radiotracer of the same lesion. The estimated radiation dose from [^{64}Cu]Cu-NOTA-trastuzumab was similar to [^{18}F]FDG and toxicities were not observed. Finally, they discovered that [^{64}Cu]Cu-DOTA-trastuzumab is efficient in evaluating disseminated disease and can detect HER2-positive metastatic BC with excellent sensitivity. A [^{64}Cu]Cu-DOTA-trastuzumab biodistribution from a 45-mg trastuzumab predose seems promising for tumor imaging, especially for the visualization of liver metastases [19], however, due to a larger liver background, the findings obtained with the administration of just the radiotracer were less than ideal [13]. Fascinatingly, both studies compared [^{64}Cu]Cu-DOTA-trastuzumab with [^{18}F]FDG PET/CT, with a maximum of 13 days in between, and revealed that some lesions could be identified only with [^{64}Cu]Cu-DOTA-trastuzumab.

Mortimer and coworkers [3] have expanded the association between tumor uptake of [^{64}Cu]Cu-DOTA-trastuzumab as measured by PET/CT and standard, immunohistochemistry (IHC)-based, histopathologic classification of HER2 status in women with metastatic BC. The finding of the study indicated that with PET maximum tumors are envisioned and after one-day injection, uptake is refelective of binding to HER2, even in patients classified as HER2 negative, which designates that trastuzumab uptake in metastatic BC is sufficiently fast, and long half-life isotopes or lag times not necessarily required. This discovery has paramount importance for PET imaging of trastuzumab regarding both patient radiation dose and clinical applicability [3].
However, the great drawback of [^{64}Cu]Cu-DOTA-trastuzumab PET/CT is that, because of the 13-h half-life of ^{64}Cu, it does not offer whole-body coverage with suitable signal-to-noise (SNR) ratio and scan duration. Nevertheless, [^{64}Cu]Cu-DOTA-trastuzumab PET can be used effectively in disseminated, HER2-positive BC when disease location is defined in move ahead by [^{18}F]FDG PET or CT [19].

The review conducted by Geraldine G. et al [1] presents available evidence and recent position of molecular imaging for the detection of HER2 (target) expression or the prediction of early treatment response in early and advanced HER2-positive BC.

There are also another radiopharmaceuticals already tested for molecular imaging for the detection of HER2. Wong k. et al [40] conducted a study to do assessment for the safety and potential of [^{64}Cu]Cu-Sarcophagine (SAR)-Bombesin PET/CT (BBN) in re-staging metastatic oestrogen receptor (ER)+/ progesterone receptor (PR)+/ (HER2-) breast BC. The study was done on 7 patients with metastatic ER+/PR+/HER2- BC undergoing staging underwent [^{64}Cu]Cu-SAR-BBN PET-CT. Their results revealed that [^{64}Cu]Cu-SAR-BBN PET/CT appears safe and may have diagnostic value in metastatic ER+/PR+/HER2- BC, mainly the lobular subtype.

Moreover, [^{64}Cu]Cu-ubiquitin is a radiolabeled form of ubiquitin, a small protein that is involved in the degradation of damaged proteins in the cell. One potential application of [^{64}Cu]Cu-ubiquitin is in cancer research, as abnormal protein degradation is a common feature of cancer cells. By tracking the distribution and degradation of proteins in cancer cells, researchers can gain insights into the underlying mechanisms of cancer and potentially develop new treatments. Li h. et al[41] demonstrated a study on the preparation and evaluation of (64Cu)-radiolabeled ubiquitin for (chemokine receptor 4) CXCR4 PET/CT imaging for mouse breast tumor. Ubiquitin has been recently identified as a (CXCR4) natural ligand, offering great potential for PET imaging of CXCR4

expression. The results suggested that (64Cu)-UbCG4 could serve as a potent PET tracer for the noninvasive imaging of CXCR4 expression in tumors.

Conclusion

The feasibility of [^{64}Cu]Cu -Trastuzumab PET/CT for identification of HER2-positive lesions were reviewed. The [^{64}Cu]Cu-trastuzumab PET/CT imaging to the diagnosis of breast cancer is both safe and feasible. [^{64}Cu]Cu -Trastuzumab may possibly be applied to select the right patients and right timing for HER2 therapy, to manage the treatment response after HER2-targeted therapy, and to detect primary or metastatic spread. The advancement of [^{64}Cu]Cu-trastuzumab PET/CT for the detection of BC is encouraging. However, more studies are required to determine the usefulness rate of imaging plans for clinical administrations.

Limitations

Our systematic review has some limitations. The number of appropriate articles was very limited, only English publications studies are considered, inadequate retrieval of previously conducted research, such as unpublished or publications in different languages.

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Conflict of interest

According to the authors, there are no conflicts of interest.

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