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European association of nuclear medicine (EANM) focus meeting 6 consensus on molecular imaging in breast cancer (endorsed by EUSOBI, ESSO, ESTRO, EuropaDonna)

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A B S T R A C T

Background: Despite significant advancements in imaging and treatment of breast cancer, clinical practice remains heterogeneous across institutions and disciplines. Molecular imaging has a pivotal role in breast cancer care, from diagnosis to recurrence assessment. To address these discrepancies and define the future direction of imaging in breast cancer, the European Association of Nuclear Medicine (EANM) convened Focus Meeting 6 on molecular imaging in breast cancer.
Methods: A three-phase consensus process was performed: 1) systematic literature review, 2) modified two-round online Delphi survey, 3) in-person consensus conference. Twenty-seven multidisciplinary experts participated in the online Delphi (nuclear medicine, radiology, medical oncology, surgery, pathology, and radiation oncology); 121 in the in-person consensus conference; patient advocacy was incorporated in the last two stages.
Results: A total of 92 statements across six thematic tracks were evaluated. Consensus was achieved on 84 statements (91 %), including areas of agreement, disagreement, and uncertainty. Key findings supported the utility of [^{18}F]FDG PET/CT at baseline staging, therapy response assessment, and recurrence evaluation, particularly in specific breast cancer subtypes. A shared call for standardising imaging interpretation, harmonising clinical and imaging guidelines, and promoting prospective multicentric studies with patient involvement emerged.
Conclusions: This EANM Focus Meeting represents the first multidisciplinary consensus on molecular imaging in breast cancer. It establishes expert-endorsed recommendations, identifies research gaps, and emphasises the need for integrated imaging and clinical strategies to improve patient outcomes and care standardisation globally.

1. Background

Breast cancer is the most prevalent cancer in women worldwide, one of the leading causes of cancer-related morbidity and mortality, and a major global health concern. According to the Global Cancer Observatory (GLOBOCAN) statistics report from 2022, breast cancer was the second most frequently diagnosed cancer (after lung cancer), and the fourth cause of death (after lung, colorectal and liver cancers) globally, regardless of gender, and the leading cause of death in women. [1] Breast cancer is predicted to increase to over 3 million new cases and 1 million deaths every year by 2040 because of population growth and ageing alone. [2].

Breast cancer is a heterogeneous disease, being categorised in subtypes that are relevant for selection of therapy and prognosis. [3,4] Molecular markers like estrogen receptor and HER2 status have become essential for breast cancer management and are now included in the latest AJCC Cancer Staging Manual. [5] As a result, breast cancer staging no longer depends solely on the TNM stage, but also considers molecular marker expression. [5]Since PET/CT and PET/MR with various radiopharmaceuticals can assess both TNM stage and molecular marker expression, nuclear medicine is especially well suited for breast cancer imaging. Despite the increasing developments in diagnosis, treatment, and monitoring, there are discrepancies in clinical practice, and there is a lack of consistency in the optimal utilisation of [^{18}F]FDG PET/CT among published guidelines. [6] These need to be considered from a multidisciplinary perspective and based on available evidence to improve patient care and outcomes.

The European Association of Nuclear Medicine (EANM) considers Nuclear Medicine as playing an essential role in patients with breast cancer and devoted its 6th Focus Meeting to this topic under the motto: “Shaping the Future of Breast Cancer Care with Molecular Imaging”.

2. Aims of the EANM focus meeting 6

1. To define the role of imaging in breast cancer, particularly the utility of nuclear medicine techniques in different clinical settings (including initial systemic staging, assessment of response to therapy, and detection of recurrence).
2. To reach a multidisciplinary consensus on the current state of the art in nuclear medicine imaging in breast cancer.
3. To generate expert recommendations on how best to guide professionals in their clinical decisions beyond the existing guidelines.
4. To identify knowledge gaps and topics with lack of scientific evidence for potential future studies.

3. Methods

To meet the project aims a cross-sectional iterative process to explore opinions and reach consensus was completed. This process consisted of three phases 1) a systematic literature review, informing 2) a modified online Delphi survey, followed by 3) a consensus conference (methods details of all stages are provided as supplementary material, with some key details conveyed below).

The expert panellists of this Focus Meeting were purposefully sampled [7] to represent relevant clinical expertise. The criteria were confirmed membership of a relevant professional society and/or expertise in the topic via published research or guidelines.

Delphi methodology was selected because it enables a panellist’s participation in their own time and facilitates anonymised between-round feedback, whilst avoiding the undue influence of dominant or authoritative voices. [8–10] We report this phase of the study following the Delphi Standards for Reporting guidance (DELPHISTAR), [11] included in supplementary file 4.

A subgroup of four members of the expert panel (SV, FC, KG, PAA)

constituted the study steering group. This study steering group first created a list of statements based on the literature review from phase 1 and their expert knowledge. This process generated 92 statements across the six tracks, with which panellists could agree or disagree.

The Delphi was administered in 2 rounds using Welphi, [12] a web-based Delphi-specific software programme. Panellists were invited to participate in round 1 via an email from the EANM central office. This email contained a link to the survey and the literature review. Informed consent was implied by the participant submitting the Delphi results. Panellists were asked to score each statement on a 1 (strongly disagree) to 9 (strongly agree) Likert scale, with an 'unable to score' option. Panellists were encouraged to give feedback to the steering group and to propose any statements they felt should be added for scoring by all panellists in round 2 or other amendments, such as clarifying existing statements. No statements were added in round 2 but there were some minor clarifications – these new edits were flagged clearly for participants.

3.1. Delphi - analysis

The analysis method proposed by the RAND corporation was selected [13] because it has been shown to be stable in relatively small panels. [13] This method utilises the median and the 30th-70th interpercentile range (IPR) and IPR adjusted for symmetry (IPRAS) for each statement. IPRAS is calculated as 2.35 + [asymmetry index * 1.5], with asymmetry being defined as the absolute difference between the central point of the IPR and five (the scale mid-point). If the IPR > IPRAS then this is interpreted as 'no consensus', whereas the opposite is categorised as 'consensus'. Microsoft Excel [14] was used for all analysis. Median scores in the range 1–3 were categorised as 'disagree', 4–6 as 'uncertain', and 7–9 as 'agree'. A worked example is shown in supplementary file 5 using data from this project. The number choosing 'unable to score' was noted for each statement.

This scientific initiative was promoted by the EANM and was endorsed by the European Society of Breast Imaging (EUSOBI), the European Society of Surgical Oncology (ESSO), European Society for Radiotherapy and Oncology (ESTRO), and the European patient's representative coalition EuropaDonna. The EANM Focus Meeting 6 was principally funded by the EANM, with supplementary funding provided through unrestricted grants from Novartis and ABSCINT. The funders had no influence over the design, data, analysis, interpretation and writing recommendations.

This Focus Meeting was organised in six thematic 'tracks':

1. General aspects about PET/CT
2. Assessing Suspicious Breast Lesions with Imaging (T&N Staging)
3. Baseline Systemic Staging of Breast Cancer (M Staging)
4. Assessing Systemic Treatment Response with Imaging
5. Assessing Systemic Recurrence with Imaging
6. Future Imaging Challenges & Developments in Breast Cancer

4. Results and discussion

The panellists included 27 representatives from medical specialities in the field of breast cancer and one patient representative from EuropaDonna (details are provided in Table 1 of supplementary material). Of the 27 clinical experts invited to participate in the Delphi survey, 24 completed both rounds and three did not participate, and all 27 experts plus the patient representative contributed to the consensus conference and manuscript writing process.

4.1. Systematic literature review

A total of 124 records were included, and there was no discernible difference in the proportion of systematic reviews rated at low, moderate, and high quality across tracks. The complete results of the systematic literature search and AMSTAR2 results are reported in supplementary file 1.

4.2. Modified Delphi survey and consensus conference

There was consensus on 84/92 (91 %) statements after round two. Eight statements had no consensus (five of these were about the use of sestamibi breast scintigraphy, statements n° 32 to 36). For five statements, the median score was 5, indicating that the panel did 'neither agree nor disagree' and necessitating further discussion at the consensus conference.

In the onsite consensus conference, there were 121 participants (excluding panellists and patient representative), representing 31 countries, mostly from Europe (The Netherlands and Spain corresponding to 13 % each), but also from the United States of America, Canada, Australia and Costa Rica. The male/female ratio was 1/1.6.

The key messages from the whole Focus meeting 6 is summarised Table 1.

A flow diagram summarising the whole consensus process is shown in Fig. 1.

The Delphi results and consensus discussions are summarised in the section below. For each track, a table containing the statements, median,

Table 1
Summary of key messages discussed during the Focus meeting 6, organised by clinical setting.

→ Baseline loco-regional staging

- Radiologic modalities are the most appropriate. Sestamibi breast scintigraphy (SBS) is useful when MR is not possible.
- Sentinel Lymph Node Biopsy (SLNB) has similar results when the learning curve is achieved, regardless of the protocol. There is a trend toward sparing axillary surgery and relying on imaging axillary staging, though SLNB remains the standard in the majority of current clinical practice.

→ Baseline systemic staging

- [^{18}F]FDG PET/CT is useful in patients with clinical stage ≥ IIB, regardless of breast cancer subtype. Its role is even more important in oligometastatic disease. [^{18}F]FDG PET/CT should be considered an alternative to the combination of contrast enhanced chest-abdominal-pelvic CT and bone scan.
- To image the central nervous system (CNS) and liver, MR is the preferred modality.
- When available, [^{18}F]FDG PET/MR is preferred over [^{18}F]FDG PET/CT, particularly in lobular breast cancer.
- [^{18}F]FDG was the preferred initial radiopharmaceutical to be used in ER+ breast cancer. When indeterminate clinical/imaging findings persist, [^{18}F]FES could be performed.

→ Treatment response and recurrence

- The same imaging modality should be used at the baseline evaluation and after treatment to assess treatment response more accurately.
- Radiological breast imaging is recommended to identify residual primary tumour at the end of treatment.
- [^{18}F]FDG PET/CT has a role in monitoring treatment response in the metastatic setting. PET should be reported according to PERCIST or EORTC criteria.

→ Follow-up

- Annual mammography (MG) and, depending on additional risk factors, supplemental breast magnetic ressonance (MR) is recommended
- [^{18}F]FDG PET/CT is recommended whenever there is clinical, laboratory or imaging suspicion of recurrence. It should be performed to confirm oligometastatic disease. It is the preferred modality for radiation therapy planning in oligometastatic disease outside of the CNS and liver.

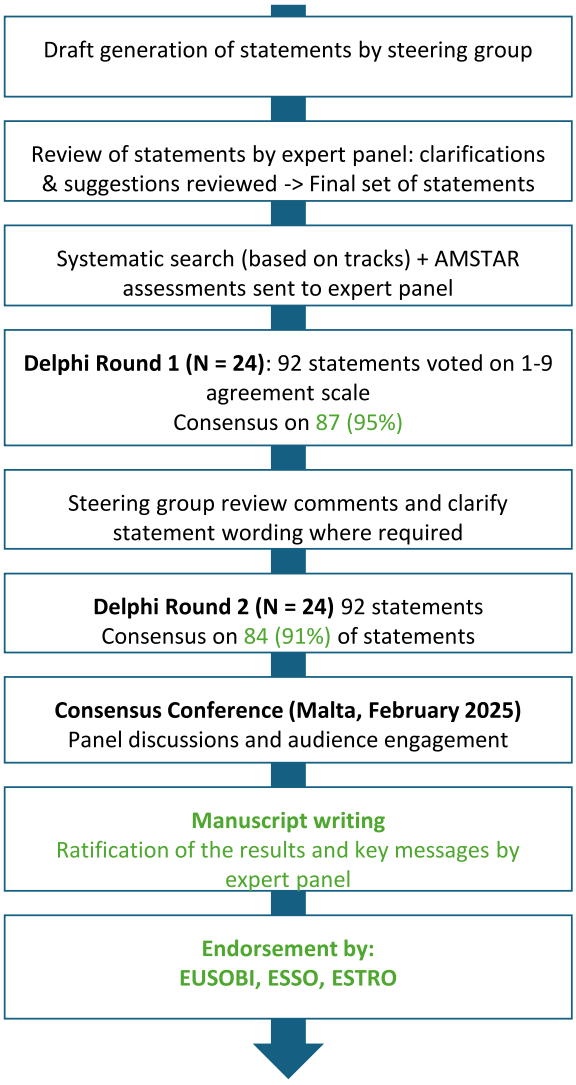

Fig. 1. Summary of Focus 6 consensus process.

30th and 70th percentiles, and the percentage of participants scoring in the 7–9 range, after the second online voting round, results interpretation and number of panellists unable to score is presented. The text below the table provides a concise overview of the "consensus to agree", the main reasons for the statements "consensus to disagree", and a of summary from the live discussion for the statements "consensus to neither agree nor disagree" and "no consensus". Complementary information discussed during the conference is also summarised in tables.

4.3. Track 0 – general aspects

Track 0 included 24 statements. After the second online Delphi round the scores were: 21 consensus to agree, 2 consensus to neither agree nor disagree, and 1 no consensus (Table 2).

4.3.1. Consensus to agree

Panellists unanimously agreed that consensus statements approved by clinical experts should be discussed with patient advocates and are important to guide and disseminate best practices. Scientific evidence, guidelines, and experience are factors likely to influence physician willingness to refer a patient for PET.

When requesting [^{18}F]FDG PET/CT, a specific question to be clarified with the PET imaging should be asked, and complete information about the patient and the disease should be provided to optimise the study. [15] Whenever possible, [^{18}F]FDG PET/CT should be done at least 3 months after surgery, at least 10 days (15 days if possible) after the last dose of chemotherapy or endocrine therapy, and at least 3 months after the last session of radiation therapy to avoid false positive and negative findings. [16] Due to the limited evidence, these premisses are mainly based on expert opinion, and according to the most recent joint EANM/SNMMI guidelines about [^{18}F]FDG PET/CT in no special type (NST) breast cancer. [16] In the specific case of [^{18}F]FES PET/CT, medication blocking oestrogen receptors should be withdrawn for a certain period before the exam to optimise imaging quality (details in statement n°18). [17,18].

It was mentioned that [^{18}F]NaF PET/CT is more accurate than bone scan to detect bone metastasis. However, [^{18}F]FDG PET/CT is preferable to [^{18}F]NaF PET/CT because it enables the simultaneous detection of bone and visceral metastases. [19].

Regarding PET/CT acquisition, there was overall agreement regarding the advantage of using high-dose/fully diagnostic contrast enhanced CT. [20] Nevertheless, it was recognised that low dose non-contrast enhanced CT was still the most frequently used in clinical practice in the majority of countries represented during the conference. Despite potential artifacts related with the inclusion of the head in the standard FOV and, after assessing the potential risk-benefit balance, it may be useful to detect major lesions and, therefore, extract additional information from the whole-body scan. Whenever there are significant doubts regarding the PET/CT findings, a dedicated head acquisition may be made to improve imaging. If there is suspicion of brain lesions, MR is recommended (statement n° 12).

PET/CT images should be reconstructed according to EANM Research GmbH (EARL) recommendations [21,22] as a basis for a standardised image quality and SUV quantification, especially in clinical trials. It may not provide the best achievable image quality and resolution, particularly when using novel long-axial field of view (LAFOV) or total body PET/CT scanners. Nevertheless, limited studies show similar results when using EARL in LAFOV PET/CT scanners. [23].

When evaluating a pregnant woman with breast cancer, ultrasound (US) is the recommended method for initial evaluation. Mammography (MG) [24] can be safely performed during pregnancy whenever necessary. [25] Breast MR may be performed considering that, according to the ESUR guidelines on contrast agents, [26] the smallest possible dose of a macrocyclic gadolinium contrast agent may be given, when there is a very strong indication for enhanced MR. For systemic staging, wbMR is the recommended method, when available. If there is a clinical benefit for PET, PET/CT can be safely performed (statement n° 22) [27,28], but PET/MR is preferred whenever possible. [29,30] Similarly, [26] iodine-based contrast may be administered when a radiographic examination is essential.

Finally, it was discussed that imaging findings that may significantly interfere with a patient's quality of life and potentially be life-threatening should be rapidly transmitted to the referring physician and that imaging results should be discussed at the breast multidisciplinary tumour board.

4.3.2. Consensus to neither agree nor disagree

Statement n°4, "Patient's preference is a factor that is likely to influence my willingness to refer a patient for PET (assuming that availability is unlimited)", was rephrased according to EuropaDonna's suggestion as "Patient's request, irrespective of clinical need, is a factor that is likely to influence my willingness to refer a patient for PET (assuming that availability is not an issue)". This new statement was voted onsite, but did not reach agreement. The result reflected the fact that clinicians usually prescribe examinations according to clinical indications and not at request of the patient. The importance of patient involvement in clinical decision-making and the need to provide updated and clear information to the patients was nevertheless also emphasised.

Panellists tended to disagree on statement n° 7, "Costs-related

Table 2
Track 0 Delphi results.

Statement	Median	30th Percentile	70th Percentile	Percent choosing 7, 8, or 9	Interpretation	N choosing unable to score
1. Although consensus statements cannot replace high-level evidence, they are important to help guide and disseminate best practices from centres of excellence to the wider clinical community.	9	9	9	96 %	Consensus agree	0
2. Consensus statements agreed by clinical experts should be discussed with patient advocates.	9	7	9	92 %	Consensus agree	0
3. Incorporation into guidelines is a factor likely to influence my willingness to refer a patient for PET (assuming that availability is unlimited).	9	8	9	96 %	Consensus agree	2
4. Patient's preference is a factor that is likely to influence my willingness to refer a patient for PET (assuming that availability is unlimited).	5	4	7	35 %	Consensus neither agree nor disagree	1
5. Evidence of benefit from scientific literature is a factor that is likely to influence my willingness to refer a patient for PET (assuming that availability is unlimited).	9	9	9	100 %	Consensus agree	1
6. Personal experience is a factor that is likely to influence my willingness to refer a patient for PET (assuming that availability is unlimited).	7	6	7	64 %	Consensus agree	2
7. Costs-related aspects are likely to influence my willingness to refer a patient for PET (assuming that availability is unlimited).	6	4	6	22 %	Consensus neither agree nor disagree	1
8. PET/CT images should be reconstructed according to EANM Research GmbH (EARL) recommendations in order to be more homogeneous and comparable even if acquired with different equipment.	9	7	9	82 %	Consensus agree	2
9. PET with EARL reconstructions may be particularly useful for comparison studies during treatment, in clinical trials and include artificial intelligence (AI)-based imaging analysis.	9	9	9	86 %	Consensus agree	4
10. To optimise PET/CT the CT component should be high dose/fully diagnostic.	8	7	9	71 %	Consensus agree	0
11. To optimise PET/CT contrast should be used whenever necessary.	9	8	9	83 %	Consensus agree	1
12. The inclusion of the head in the PET/CT field of view (FOV) improves staging.	7	6	7	52 %	Consensus agree	1
13. In case of equivocal uptake, delayed acquisition of specific body segments should be acquired (ex. delayed images of the liver in [^{18}F]FDG PET/CT).	7	4	8	50 %	No consensus	3
14. When prescribing [^{18}F]FDG PET/CT, the clinician should provide complete information regarding staging, therapy and clinical problems and posing a question to be clarified with the PET imaging.	9	9	9	100 %	Consensus agree	1
15. Whenever possible, [^{18}F]FDG PET/CT should be done at least 3 months after surgery, to avoid false positive findings.	7	7	8	74 %	Consensus agree	1
16. When assessing response to systemic therapy, [^{18}F]FDG PET/CT should be done at least 10 days (15 days if possible) after the last dose of chemotherapy or endocrine therapy, to avoid the effects of the flare phenomenon or stunning reaction.	7.5	7	9	79 %	Consensus agree	0
17. When assessing response to radiation therapy, [^{18}F]FDG PET/CT should be done at least 3 months after the last treatment.	8	8	9	96 %	Consensus agree	1
18. If not compromising patient treatment, medication blocking oestrogen receptors should be withdrawn during a certain period before [^{18}F]FES PET/CT to optimise imaging quality (ex. tamoxifen and fulvestrant should be discontinued for 8 and 24 weeks, respectively. However, novel oral SERDs, such as elacestrant and rintodestrant should be discontinued for one week).	8	7	8	79 %	Consensus agree	5
19. Sodium Fluoride ([^{18}F]NaF) PET/CT is more accurate than bone scan to detect bone metastasis.	8	7	8	86 %	Consensus agree	2
20. Usually [^{18}F]FDG PET/CT is preferable to [^{18}F]NaF PET/CT because it enables the simultaneous detection of bone and visceral metastases.	9	9	9	100 %	Consensus agree	0
21. wbMR is the recommended staging method in pregnant women.	8	6	9	68 %	Consensus agree	2
22. [^{18}F]FDG PET can be safely performed in pregnant women if measures to reduce the dose to the foetus are adopted (ex. Whenever possible perform PET/MR instead of PET/CT, use digital PET equipment, low dose CT and urinary bladder catheterisation).	7	7	8	91 %	Consensus agree	1
23. All imaging findings which may significantly interfere with the patient's quality of life and potentially be life-threatening should be transmitted to the referential physician according to the local institutional critical finding's communication procedure (ex. lesion of midbrain, pneumothorax, severe vascular thrombosis, severe ascites, severe pneumonitis, mediastinal mass compressing vital/important structures).	9	9	9	100 %	Consensus agree	1
24. Proper discussion of imaging findings at the breast multidisciplinary tumour board is recommended, and it should be based on the patient's wellbeing.	9	9	9	96 %	Consensus agree	1

aspects are likely to influence my willingness to refer a patient for PET (assuming that availability is unlimited)", because generally PET is requested when there is a specific clinical indication and it is expected to provide useful information for the patient management.

4.3.3. No consensus

In cases of equivocal radiopharmaceutical uptake, delayed acquisition of specific body segments may be acquired to reduce physiological background or correct any previous artifacts (statement n° 13).

Nevertheless, there is not robust literature to support its routine use in clinical practice and extra scanning acquisitions may be difficult to include in busy departments.

4.4. Track 1 – Assessing Suspicious Breast Lesions with imaging (T&N staging)

Track 1A) about US, MG, CEM, MR and SBS included 12 statements. On 7 statements, consensus to agree was reached, and 5 had no consensus (Table 3).

Track 1B) about Lymphoscintigraphy included 12 statements. Eleven reached consensus to agree and there was 1 consensus to neither agree nor disagree (Table 3).

4.5. Track 1A) – Assessing Suspicious Breast Lesions with imaging (T&N staging)

4.5.1. Consensus to agree

There was overall agreement that for local staging bilateral US and MG and/or DBT should be the first-line imaging modalities to identify and characterise breast lesions. Supplemental imaging with CEM or breast MR can be considered. [31,32]. It was consensual that SBS may be considered when MR is not possible, as supported by the "SNMMI and EANM Procedure Standard/Practice Guideline" [33] and the "Appropriate Use Criteria for Molecular Breast Imaging in gamma-cameras". [34].

With regard to lymph node staging, axillary US is recommended in patient newly diagnosed with breast cancer to differentiate between cN0 versus cN+, and it is particularly important in patients treated with neoadjuvant systemic therapy. [31,32,35] The concept of de-escalation in lymph node surgery was also discussed to emphasise that in some patients with early cN0 breast cancer treated with breast-conserving therapy, further axillary surgery may be avoided, according to results demonstrated by several clinical trials (e.g. SOUND, INSEMA, BOOG 2013–08, NAUTILUS). [36–40].

4.5.2. No consensus

Five statements (n° 32, 33, 34, 35 and 36) did not reach consensus after 2 online voting rounds and onsite discussions, reflecting the low level of evidence available and the reduced use of SBS in clinical practice.

4.6. Track 1B) – Assessing Suspicious Breast Lesions with imaging (T&N staging): Lymphoscintigraphy

4.6.1. Consensus to agree

SLNB is recommended in early invasive breast cancer without evidence of axillary metastasis [32,41], in ductal carcinoma in situ (DCIS) proposed for mastectomy and may be appropriate in patients with oligometastatic disease treated with curative intent. [41] Despite the variability in SLN injection protocols, results are similar and was mentioned that the simplest, cheapest and fastest method should be considered the best option, depending on the institutional availability and protocols. Regarding the use of dual-tracer (statement n°42), the group discussed that results are overall similar regardless of the tracer and technique (being either radiopharmaceutical, blue dye, magnetic or fluorescent agent used alone or in combination (including hybrid tracer variants)) and the neoadjuvant or adjuvant setting, because results are mainly dependent on physician experience. [42,43].

Clinically positive nodes proposed for neoadjuvant systemic treatment should be marked with wireless technique to enable a combined procedure of SLNB with removal of marked lymph nodes. Despite the variety of localisation techniques available, after the learning curve is accomplished, results are similar regardless of whether clips, magnetic seed, radioactive-, radar- or radiofrequency-based agents are used. The decision depends on tumour and patient characteristics and the available resources at each centre.

It is recommended to assess response to neoadjuvant therapy with the same imaging modality used in the initial diagnosis. After neoadjuvant systemic treatment, SLNB is recommended in patients with cN1 disease that were downstaged to cN0 to avoid axillary lymph node dissection (ALND). [41,44,45] When conversion of cN + to N0 is observed, ALND can be spared. [46–48] Moreover, there are ongoing trials for omitting axillary surgery in selected patients with cN0 submitted to neoadjuvant systemic treatment (NAST). [49,50] Two prospective single-arm ongoing trials (EUBREAST-01 - NCT04101851 and ASICS - NCT04225858) will include patients with high likelihood of having a pCR after NAST (triple-negative or HER2-positive breast cancer), in whom the type of surgery will be defined according to the response to NAST rather than on the classical T and N status. [51].

4.6.2. Consensus to neither agree nor disagree

In the onsite conference there was a tendency to agree that "SLNB may be omitted in small breast cancer ($\leq$2 cm) and clinically negative axilla". This concurs with the results from the SOUND and INSEMA trials, which revealed that the omission of axillary surgery was non-inferior to SLNB in patients with breast cancer lesions measuring up to 2 and 5 cm, respectively, and negative preoperative axillary US. [52,53].

Complementary information about Track 1B) is provided in Table 4.

4.7. Track 2 – Baseline Systemic Staging of Breast Cancer (M staging)

Track 2 included 11 statements: 8 consensus to agree, 1 consensus to disagree, and 2 consensus to neither agree nor disagree (Table 5).

4.7.1. Consensus to agree

According to the most recent guidelines and extensive literature, it was agreed that [^{18}F]FDG PET/CT is recommended in the systemic staging of patients with NST breast cancer and clinical stage $\geq$ IIB, especially triple negative and HER2-positive. [16] Furthermore, it is useful in the initial staging of patients with NST breast cancer and clinical stage < IIB if equivocal findings are reported on CT/bone scan. [^{18}F]FDG PET/CT can be performed as an alternative to the combination of contrast enhanced chest-abdominal-pelvic CT and bone scan, particularly when using diagnostic contrast-enhanced CT. Considering that [^{18}F]FDG PET/CT is widely available in cancer centres, and data shows its impact on prognosis, survival, and costs, [16,55–57] it was agreed on the importance of having joint clinical and imaging guidelines to homogenise clinical practice. [58].

In the specific context of oligometastatic disease, both clinical and imaging guidelines agree on the usefulness of [^{18}F]FDG PET/CT to improve patient selection for targeted treatment. [16,31,59,60].

According to ESMO, NCCN and ABC guidelines, panellists agreed that brain imaging with MR or CT should be done only in symptomatic patients regardless of the staging and that the staging of patients with lepto-meningeal dissemination should include full spine imaging with contrast-enhanced MR. [31,59,60].

There was overall agreement that, when available, [^{18}F]FDG PET/MR is preferred over [^{18}F]FDG PET/CT, for systemic staging, particularly in lobular breast cancer. [61,62].

It was discussed that [^{18}F]FES may be useful in estrogen-positive breast cancer, of whether it is lobular or NST histology. The main clinical indications for [^{18}F]FES include the assessment of lesions that are difficult to biopsy or when biopsy is nondiagnostic, therapy guidance at initial presentation of metastatic disease (ex. IMPACT [63] and ET-FES [64] trials) or after progression of metastatic disease, and detection of ER-expressing breast cancer sites when other imaging modalities present equivocal or suggestive results. [17,65,66].

The sequence to perform [^{18}F]FDG and [^{18}F]FES in estrogen-positive breast cancer was highly debated due to the recent publications showing that most lobular metastases are visible on [^{18}F]FDG [67] and that [^{18}F]FDG and [^{18}F]FES have similar sensitivity for detecting lobular

Table 3
- Track 1A and 1B Delphi results.

Statement	Median	30th Percentile	70th Percentile	Percent choosing 7, 8, or 9	Interpretation	N choosing unable to score
Track 1.A) Assessing Suspicious Breast Lesions with Imaging (T&N Staging): Ultrasound (US), mammography (MG), contrast enhanced mammography (CEM), magnetic resonance (MR) and Sestamibi breast scintigraphy (SBS) (or similar lipophilic cations)						
25. US and MG and/or digital breast tomosynthesis (DBT) should be the first line breast imaging modalities to identify breast lesions.	9	9	9	100 %	Consensus agree	0
26. US and MG should be the first line breast imaging modalities to characterise breast lesions as benign or malignant.	9	9	9	100 %	Consensus agree	0
27. Breast MR or contrast enhanced mammography (CEM) should be the second line imaging modality, after US and MG, when there is disagreement between the results of clinical evaluation, MG and/or US.	9	9	9	96 %	Consensus agree	1
28. Breast MR is a concomitant first line imaging modality in specific situations (preoperatively to assess local extension of disease and rule out chest wall invasion, multifocal/multicentric or bilateral disease particularly in high-risk or lobular subtype).	9	9	9	100 %	Consensus agree	1
29. Breast MR or CEM is a concomitant first line imaging modality in specific situations (neoadjuvant setting, at baseline and at the end of systemic treatment to assess response).	9	9	9	100 %	Consensus agree	2
30. Breast MR or CEM are a concomitant first line imaging modality in specific situations (young women, baseline evaluation of women with dense breasts and routine assessment of high-risk genetic mutation carriers).	9	9	9	95 %	Consensus agree	2
31. Positron Emission Mammography (PEM) should be preferred over breast scintigraphy whenever available, based on its higher diagnostic accuracy.	8	8	8	84 %	Consensus agree	6
32. SBS is a well-established complementary imaging modality after equivocal/negative MG or MR in patients presenting as high risk for breast cancer.	7	4	8	52 %	No consensus	1
33. SBS is a well-established complementary imaging modality after equivocal/negative MG or MR in patients presenting high risk of loco-regional recurrence.	4	2	8	41 %	No consensus	2
34. SBS may be indicated in the presence of microcalcification cluster when radiological imaging is equivocal.	6	3	8	48 %	No consensus	3
35. SBS may be indicated in very dense or fibrotic (post-RT) breast when radiological imaging is equivocal.	6.5	4	8	50 %	No consensus	2
36. SBS may be indicated in presence breast devices when radiological imaging is equivocal.	7	3	8	53 %	Consensus agree No consensus	5
Track 1B) - Assessing Suspicious Breast Lesions with Imaging (T&N Staging): Lymphoscintigraphy						
37. Sentinel lymph node biopsy (SLNB) may be omitted in selected small breast cancer ($\leq$2 cm) and clinically negative axilla.	6	5	7	43 %	Consensus neither agree nor disagree	1
38. SLNB is recommended in early breast cancer and clinically negative axilla (stage $\leq$ IIB).	9	8	9	100 %	Consensus agree	1
39. SLNB is recommended in ductal carcinoma in situ (DCIS) proposed for mastectomy.	8	7	9	83 %	Consensus agree	1
40. SLNB is recommended in patients with N1 disease that were downstaged to N0 after neoadjuvant systemic treatment.	9	8	9	91 %	Consensus agree	1
41. Clinically positive nodes proposed for neoadjuvant systemic treatment should be marked with carbon/clip to enable a combined procedure of SLNB with removal of marked lymph nodes.	9	9	9	91 %	Consensus agree	1
42. Dual-tracer technique (radiopharmaceutical + coloured dye or radiopharmaceutical + fluorescent dye) should be the recommended method for SLNB. However, during the onsite meeting it was agreed that approved tracers can be used alone with similar oncological outcomes, as explained in the text.	8	7	9	83 %	Consensus agree	1
43. Both [^{99m}Tc]nanocolloids (5–100 nm) and [^{99m}Tc]tilmanocept (3–30 nm) can be used in lymphoscintigraphy, if the time between the injection and surgery is adapted to the radiopharmaceutical (due to smaller particle size and consequently fast clearance of the [^{99m}Tc]tilmanocept, surgery should be done in the same day of its injection preferably).	7.5	7	9	89 %	Consensus agree	6
44. When [^{18}F]FDG PET/CT is performed at initial staging, the number, SUVmax, dimensions and axillary level of hypermetabolic axillary lymph nodes should be reported for improving clinical decision making.	9	9	9	96 %	Consensus agree	1
45. [^{18}F]FDG uptake in axillary lymph nodes needs to be histologically confirmed, as increased uptake on [^{18}F]FDG PET/CT does not confirm axillary involvement.	9	8	9	96 %	Consensus agree	0
46. SLNB is still indicated even when there is no [^{18}F]FDG uptake in axillary lymph nodes.	9	9	9	100 %	Consensus agree	0
47. Lymphoscintigraphy (without coloured dye) can be safely performed in pregnant women, using low activities and surgery on the same day.	9	8	9	90 %	Consensus agree	4
48. Radio-guided occult lesion localisation (ROLL) and sentinel node and occult lesion localisation (SNOLL) are valuable options in case of difficulties to mark the breast lesion with other techniques (such as wire and carbon).	7	7	8	75 %	Consensus agree	9

Table 4
Complementary information about Track 1B).

Complementary information about Track 1B)
• [^{99m}Tc]Tc-tilmanocept has been withdrawn from Europe, so [^{99m}Tc]Tc-nanocolloids are the only available radiopharmaceuticals for SLN in Europe (statement n° 43).
• The necessity of including metabolic parameters when reporting axillary lymph nodes on [^{18}F]FDG PET/CT was controversial (statement n°44). SUV_{max} and SUV_{mean} were the more relevant parameters, but the need to specify the threshold and the imaging reconstruction protocol (EARL-based or local protocol) was discussed. It was agreed that the analysis of the number of lymph nodes with uptake higher than the background should follow the anatomic regions and number counts according to the TNM criteria. [54]
• It was unanimously agreed that [^{18}F]FDG uptake in axillary lymph nodes needs to be histologically confirmed (statement n° 45). In cases where there is high metabolic suspicion of lymph node involvement, but it is not confirmed, or there is no inflammatory explanation on biopsy, it is recommended to discuss the case in the multidisciplinary tumour board and to perform second-look biopsy considering the location reported on [^{18}F]FDG PET/CT.

Table 5
Track 2 Delphi results.

Statement	Median	30th Percentile	70th Percentile	Percent choosing 7, 8, or 9	Interpretation	N choosing unable to score
49. Conventional staging with chest-abdominal-pelvic ceCT and bone scan is recommended in the initial staging of stage ≤ IIA regardless of the molecular subtype.	2	1	3.4	13 %	Consensus disagree	1
50. [^{18}F]FDG PET/CT is recommended in the systemic staging of patients with NST BC and clinical stage ≥ IIB.	9	8	9	96 %	Consensus agree	0
51. [^{18}F]FDG PET/CT is recommended in the initial staging of patients with NST BC and clinical stage < IIB if equivocal findings are reported on CT/bone scan.	9	7	9	96 %	Consensus agree	0
52. [^{18}F]FDG PET/CT can be performed as alternative to chest-abdominal-pelvic CT and bone scan.	9	9	9	96 %	Consensus agree	0
53. Brain imaging with MR or CT should be done only in symptomatic patients regardless of the staging.	9	8	9	78 %	Consensus agree	1
54. Staging of patients with lepto-meningeal dissemination should include full spine imaging with contrast-enhanced MR.	9	9	9	96 %	Consensus agree	0
55. [^{18}F]FDG PET imaging can be performed in the staging of patients with locally advanced lobular BC to verify appropriate use of [^{18}]F-FDG during patient follow-up. In case of no abnormal [^{18}]F-FDG uptake, conventional imaging modalities (CT scan and bone scan) should be used instead because the cancer may be non-avid for [^{18}F]FDG.	8	7	8	79 %	Consensus agree	0
56. When available, [^{18}F]FDG PET/MR is preferred over [^{18}F]FDG PET/CT in patients with lobular BC to increase the detection of low [^{18}F]FDG-avid lesions using MR sequences (particularly diffusion restriction).	7	6	7.7	64 %	Consensus agree	2
57. Whenever available, PET/CT with [^{18}F]FES may be performed for proper staging of locally advanced lobular BC.	7	7	8.1	75 %	Consensus agree	0
58. Whenever available, PET/CT with [^{89}Zr]trastuzumab may be used to stage locally advanced HER2-positive BC.	5.5	3	6	17 %	Consensus neither agree nor disagree	2
59. Whenever available, PET/CT with [^{89}Zr]anti-PD1/PD-L1 may be used to stage locally advanced triple negative BC.	5	3	6	13 %	Consensus neither agree nor disagree	2

metastases. [68] Considering the broader availability of [^{18}F]FDG and lower costs, it was advocated that [^{18}F]FDG was the preferred initial radiopharmaceutical to be used, and [^{18}F]FES may be performed in case of indeterminate findings.

4.7.2. Consensus to disagree

Panellists disagreed on statement n° 49 ("Conventional staging with chest-abdominal-pelvic ceCT and bone scan is recommended in the initial staging of stage ≤ IIA regardless of the molecular subtype") because, in early/localised breast cancer (non-inflammatory and without high risk), additional imaging studies should only be considered if there is suspicion of metastases. [31,32] Furthermore, it was recognised that bone scans presented lower sensitivity compared to [^{18}F]FDG PET/CT. [19].

4.7.3. Consensus to neither agree nor disagree

There was uncertainty regarding statement n° 58 ("Whenever available, PET/CT with [^{89}Zr]trastuzumab may be used to stage locally advanced HER2-positive BC") because the use of anti-HER2 tracers has not been implemented in clinical practice due to the challenging radiopharmaceutical production and limited availability. Nevertheless, several papers have shown promising results to evaluate the whole tumour burden, including inter and intra-lesion heterogeneity, to better select patients and to predict response to therapy. This information is not provided through immunohistochemistry analysis because biopsy may not be a reliable reflection of the status of the entire tumour lesion. Robust evidence on the role of HER2 imaging has been demonstrated to assess HER2 heterogeneity in advanced breast cancer (IMPACT trial), [69] reveal lesions with a higher chance to be HER2 positive on IHC (Hermia study), and predict upfront HER2 positive patients not responding to the antibody drug conjugate T-DM1 (ZEPHIR 1 trial). [70, 71] Additional studies are ongoing to improve tailoring the highly active, but also toxic, new generation of antibody-drug conjugates (ADC), such as the role of HER2 imaging before T-DXd (Oasis project) and after T-DXd (Zephir 2). Expectations towards the use of nanobodies due to their fast biokinetics, together with simpler manufacturing procedure or commercialisation, are increasing. [72–75].

There was also consensus to neither agree nor disagree on statement n° 59 ("Whenever available, PET/CT with [^{89}Zr]anti-PD1/PD-L1 may be used to stage locally advanced triple negative BC"). It was noticed that although Pembrolizumab is the only immune checkpoint inhibitor approved for treating triple negative breast cancer, several imaging tracers labelling anti-PD1 and anti-PD-L1 have been developed. Despite literature showing promising results on the use of anti-PD-1/PD-L1-labelled radiopharmaceuticals to overcome the limitation that biopsy may not be representative of the whole tumour lesion, particularly in

lung cancer and melanoma, there are insufficient data about anti-PD-1/PD-L1-based radiopharmaceuticals in breast cancer. [76].

Complementary information about Track 2 is presented in Table 6.

4.8. Track 3 – Assessing Systemic Treatment Response with imaging

Track 3 included 16 statements organised in Track 3.A) and 3.B) about the assessment of treatment response in non-metastatic and metastatic disease, respectively. Consensus to agree was obtained in 14 statements. There was consensus to disagree and no consensus in 2 other statements (Table 7).

4.8.1. Consensus to agree

There was overall agreement that the same imaging modality should be used at baseline evaluation and after treatment to assess treatment response accurately. Although PET/CT scans should be scheduled according to the time periods referenced before (Track 0 – general aspects) whenever possible, interrupting ongoing therapy is not mandatory and should be avoided.

Panellists agreed that [^{18}F]FDG PET/CT is more specific than bone scan to address clinical osteo-articular pain suspicious for bone metastases. When evaluating response to therapy with [^{18}F]FDG PET/CT, metabolic patterns suggesting possible therapy-related adverse events should be reported.

Despite general agreement during the online voting that [^{18}F]FES PET/CT is preferred to [^{18}F]FDG PET/CT in patients with ER+ breast cancer, during the onsite meeting, it was agreed that systemic evaluation may start with [^{18}F]FDG PET and, in case of indeterminate imaging and/or clinical findings, [^{18}F]FES PET could be added. As mentioned previously in track 2, this is based on recent publications showing that [^{18}F]FDG and [^{18}F]FES have similar sensitivity for detecting lobular metastases [68], higher availability and lower costs of [^{18}F]FDG.

RECIST is currently considered the most widely used and validated method for evaluating treatment response of various solid tumours by imaging in clinical trial. [77] Despite the validation and high reproducibility of RECIST, it is not applicable in 40 % of patients with metastatic breast cancer, mainly because bone metastases often are non-measurable on RECIST (the exception being bone metastasis with lytic or soft tissue component), and sclerotic changes may be a sign of positive treatment response. [77,78] Furthermore, RECIST presents other limitations, including the long time period to show response or progression (because morphological changes usually occur after metabolic changes [78]), the stable disease category contains both responders and non-responders, and it does not report dissociated/mixed/heterogeneous response to therapy, which may impact clinical management. [79].

Regarding PET/CT, it was agreed that response assessment on PET should follow PERCIST or EORTC criteria, in both non- and metastatic disease. [80–82] In immunotherapy, PET scans should be reported according to immunotherapy response criteria (the most common being iPERCIST, imPERCIST and PERCIMT). [83] However, it was noted in the discussion meeting that PERCIST/EORTC criteria are not often used in routine clinical practice, and that the current response evaluation criteria were originally developed for use in drug trials and lack a patient-centred perspective. Considering these criteria could provide valuable information, particularly in assessing response in bone metastases and in clinical trials, the need to update and homogenise their use in order to better reflect patient-focused outcomes was highlighted. [84–86].

In daily practice, clinical evaluation of the patient provides good perception of treatment response before any imaging modality, especially in the neoadjuvant context (e.g. through breast physical examination). However, in advanced disease, tumour progression might be more subtle, not necessarily associated to a worsening of cancer-related symptoms or detectable signs at physical examination, making imaging techniques more relevant to assess treatment efficacy. Currently, biomarkers such as CA15-3 for metastatic disease and Ki67 drop in early disease, are often used in clinical practice to evaluate response to therapy. [32,59,87,88] A matter of debate is whether blood-based biomarkers would be useful to predict tumour relapses or progression earlier than imaging techniques. Results published so far showed the potential to anticipate events by using CA15-3 or ctDNA, but therapeutic implications and the impact on prognosis for earlier introduction of treatment changes remain uncertain, as well as technical limitation related to ctDNA detection.

4.9. Track 3.A) – assessment of treatment response in non-metastatic disease

In the non-metastatic setting, the main role of imaging is staging and re-staging, though it can assess treatment response in the context of neoadjuvant therapy. Radiological breast imaging (MG, CEM, MR) is recommended to identify residual primary tumour at the end of treatment. It was pointed out that MG has a limited role in NAST response assessment because it underestimates the extent of disease, subtle changes may not be visible, and it has limited sensitivity for residual disease.

Recent studies indicate that [^{18}F]FDG PET/CT shows better specificity when compared to MR, while MR presents superior sensitivity for assessing pCR after NAST. [89,90] The combination of both modalities may represent the best diagnostic tool in this setting.

[^{18}F]FDG PET has low sensitivity for detecting residual primary tumour compared to MR, because it tends to underestimate the tumour burden. Nevertheless, it presents moderate to good sensitivity (80–85 %), but lower specificity (65–80 %), [85,91,92]to predict early response to neoadjuvant therapy (as early as after the first or second cycle of treatment), particularly in triple negative and HER2-positive subtypes. Moreover, [^{18}F]FDG provides high prognostic value for disease recurrence and survival, particularly in triple negative and HER2-positive subtypes. [85,93] Therefore, new treatment strategies may incorporate [^{18}F]FDG PET/CT for therapy de-escalation. In two prospective multicenter trials (AVATAXHER [94] and PHERGain), [95,96] [^{18}F]FDG PET/CT findings were used to change neoadjuvant treatment early in the treatment course of HER2-positive breast cancer.

Good results were also reported on the Dutch multicenter trial (TRAIN-3 [97]) about therapy de-escalation with MR in stage II-III HER2-positive breast cancer.

Table 6
Complementary information about Track 2.

Complementary information about Track 2
• Circumstances to include PET tracers other than [^{18}F]FDG in systemic staging and therapy selection were discussed. Tracers other than [^{18}F]FDG may be indicated for non-FDG-avid disease; however, there is no evidence or consensus-based definition of hypometabolic lesion on [^{18}F]FDG (and no consensual definition of low uptake on FES and anti-HER2). Therefore, currently, it seems reasonable to start with [^{18}F]FDG, due to its wider availability, and then [^{18}F]FES or anti-HER2 tracers according to biopsy results. It was speculated that fibroblast activation protein inhibitor (FAPI) tracers may change this paradigm in the future.
• There is a need to homogenise imaging interpretation criteria, including [^{18}F]FES and anti-HER2 tracers, perform cost-effectiveness studies, and include these tracers in clinical guidelines. This may promote wider clinical request and agency approval allowing for improved availability and decreased cost worldwide.
• The role of [^{18}F/^{68}Ga]FAPI and, particularly anti-PD-1/L1 PET tracers, in breast cancer needs to be demonstrated further.

Table 7
Track 3 Delphi results.

Statement	Median	30th Percentile	70th Percentile	Percent choosing 7, 8, or 9	Interpretation	N choosing unable to score
60. The same imaging modality at baseline condition and after treatment should be used for treatment response assessment.	9	9	9	100 %	Consensus agree	0
61. [^{18}F]FDG PET/CT is more specific than bone scan to address clinical osteo-articular pain suspicious of bone metastases.	9	8	9	96 %	Consensus agree	0
62. Whenever possible, PET/CT scan should be scheduled according to the time periods referred before (Track 0 – general aspects), but it is not recommended to interrupt ongoing therapy for therapeutic evaluation purposes.	9	9	9	91 %	Consensus agree	1
63. When evaluating response to therapy with [^{18}F]FDG PET/CT, metabolic patterns suggesting possible therapy-related adverse events, such as pneumonitis, colitis or thyroiditis, should be reported.	9	9	9	100 %	Consensus agree	0
64. [^{18}F]FDG PET/CT is preferred to [^{18}F]FES in patients with lobular BC, due to recent publications, availability and costs[^{18}F]FES may be performed in case of indeterminate findings. (This statement was changed according to recent data published after the Delphi study)	7	5	8	61 %	Consensus agree	1
65. Whenever available, PET/CT with [^{89}Zr]trastuzumab is preferred to [^{18}F]FDG PET/CT in patients with HER2-positive BC.	3	3	7.4	35 %	No consensus	1
66. Whenever available, PET/CT with [^{89}Zr]anti-PD1/PD-L1 is preferred to [^{18}F]FDG PET/CT in patients with triple negative BC.	3	1	4.4	22 %	Consensus disagree	1
67. Response assessment on PET should be performed according to standard treatment response criteria (PERCIST or EORTC criteria) in stable metabolic disease (SMD), progressive metabolic disease (PMD), complete metabolic response (CMR) or partial metabolic response (PMR).	9	7	9	92 %	Consensus agree	0
68. In the specific case of immunotherapy, PET scans should be classified according to standard immunotherapy response criteria (the most common being iPERCIST, imPERCIST and PERCIMT) in unconfirmed progressive metabolic disease (uPMD), stable metabolic disease (SMD), progressive metabolic disease (PMD), complete metabolic response (CMR) or partial metabolic response (PMR).	9	7	9	91 %	Consensus agree	1
69. If [^{18}F]FDG PET/CT is classified as unconfirmed progressive metabolic disease (uPMD), confirmation with [^{18}F]FDG PET/CT after 4–8 weeks should be done.	8	7	9	83 %	Consensus agree	1
Track 3.A) – Assessment of treatment response in non-metastatic breast cancer						
70. [^{18}F]FDG PET is not very sensitive to reveal the residual primary tumour at the end of treatment, because it tends toward underestimation, therefore, radiological breast imaging (US or MR) is recommended in this context.	9	8	9	100 %	Consensus agree	0
71. [^{18}F]FDG PET/CT is associated with good sensitivity, but lower specificity, to predict early response to neoadjuvant therapy (as early as the first cycle of treatment), particularly in triple negative and HER2-positive subtypes.	8	7	8	91 %	Consensus agree	1
72. [^{18}F]FDG PET/CT after neoadjuvant therapy provides high prognostic value for disease recurrence and survival, particularly in triple negative and HER2-positive subtypes.	7	6	8	67 %	Consensus agree	0
Track 3.B) – Assessment of treatment response in metastatic disease						
73. [^{18}F]FDG PET/CT has a role in monitoring treatment response in metastatic NST BC, enabling early response evaluation.	9	8	9	100 %	Consensus agree	0
74. [^{18}F]FDG PET/CT is particularly useful to assess the response in bone metastases.	9	8	9	91 %	Consensus agree	1
75. Tumour response on [^{18}F]FDG PET/CT is associated with progression free survival and disease-specific survival.	9	8	9	100 %	Consensus agree	1

4.10. Track 3.B) – assessment of treatment response in metastatic disease

ESMO and ABC guidelines [59,60] recommend monitoring treatment response every 2–4 months, but longer intervals are acceptable, particularly for indolent disease, and intervals should not be shortened except for suspected disease progression.

It was agreed that [^{18}F]FDG PET/CT has a role in monitoring treatment response, enabling early response evaluation, mainly in NST breast cancer. [^{18}F]FDG PET/CT is particularly useful in assessing the response in bone metastases, superior to CT and bone scans for this indication. [78,98,99] Furthermore, tumour response on [^{18}F]FDG PET/CT is associated with better progression-free survival, disease-specific survival, and fewer skeletal-related events. [86,100–102] Although these premises are concordant with the EANM/SNMMI guidelines published in 2024, [16] ESMO guidelines from 2021 (and including the updated v1.2 April 2025) [60] provide slightly different recommendations, such as referring to bone scans as the mainstay for evaluation of bone-only/predominant metastases, but also mentioning that [^{18}F]FDG PET/CT might provide earlier guidance in monitoring bone-only/predominant metastases. ESMO guidelines [60] highlight that there is no evidence that any monitoring approach provides an overall survival benefit over another.

Despite similar diagnostic accuracy has been described between wbMR and [^{18}F]FDG PET/CT, particularly in assessing bone metastases, currently, wbMR is less widely available due to limited MR scanning capacity, longer scanning times and radiologist's expertise and training. [103].

4.10.1. Consensus to disagree and no consensus

Statements n° 65 reached no consensus and statement n° 66 was unanimously disagreed with by the panellists. The summary of the onsite discussion is that novel tracers, such as [^{18}F]FES, [^{89}Zr]anti-HER2, and [^{89}Zr]anti-PD1/PD-L1 are less suitable for response assessment but may have predictive value. Notwithstanding the need for

additional studies, some promising examples of using non-[^{18}F]FDG radiopharmaceuticals to predict response included: (1) [^{18}F]FES to assess therapy efficacy with CDK4/6 inhibitors [66,104,105] (2) low/-absent tumour [^{89}Zr]anti-HER2 uptake in HER2-positive metastatic breast cancer to predict short time to treatment failure, [70,71] and (3) potential of [^{89}Zr]anti-PD1/PD-L1 uptake to predict survival. [76].

Other topics discussed during Track 3 are summarised in Table 8.

4.11. Track 4 – Assessing Systemic Recurrence with imaging

Track 4 was composed of 9 statements, voted as: 7 consensus to agree, 1 consensus to disagree, and 1 no consensus (Table 9).

4.11.1. Consensus to agree

The frequency and affected organs of breast cancer recurrence depend on TNM stage and subtype. [106–108] During the follow-up of women with a history of breast cancer, there is an active search for local recurrence, often through annual MG. The clinical indicators of recurrence include persistent or new-onset symptoms, physical exam findings, laboratory changes and imaging findings. Early detection of local or systemic recurrence may improve the ability to treat and influence patients' quality of life and perhaps survival. [109,110] The panellists agreed that [^{18}F]FDG PET/CT is recommended whenever there is clinical, laboratory or imaging suspicion of recurrence. [^{18}F]FDG PET/CT presents high diagnostic accuracy to detect recurrence with a sensitivity, specificity, and area under the ROC curve of 1.00, 0.88, and 0.98, respectively. [111] A positive [^{18}F]FDG PET/CT provides high probability of metastases (85 %), and a negative test is able to rule out distant metastases in women with clinically suspected recurrent breast cancer. [111] It impacts clinical management in 51–69 % of patients [112] and can substitute for CT and/or bone scan in the detection of bone metastases. [84,113,114].

It was unanimously agreed that [^{18}F]FDG PET/CT should be used to confirm oligometastatic disease and is the preferred modality for radiation therapy planning in oligometastatic disease, in agreement with the recommendations from the joint EANM/SNMMI guidelines and the EORTC Imaging and Breast Cancer Groups consensus. [16,115] The IMPACT-MBC trial described the influence of tumour load and demonstrated better progression-free survival and overall survival in patients with up to 3 metastases than those with more than 3 metastases. [116].

Brain MR is the first imaging modality when there is suspicion of CNS recurrence. When there is a high suspicion of brain or liver metastases, additional organ-targeted MR should be performed to evaluate the extent of the disease in the organ. Despite underperforming in lung metastasis detection, some data state that whole-body MR (wbMR) presents similar performance to [^{18}F]FDG PET/CT in detecting systemic recurrence but has not been thoroughly investigated. It has also been advocated that [^{18}F]FDG PET/MR may be a better option than wbMR. [117].

As previously stated, [^{18}F]FDG is the preferred initial radiopharmaceutical for all subtypes, and [^{18}F]FES should be performed afterwards in case of indetermined findings. Therefore, whenever available, consider [^{18}F]FES PET/CT to complement [^{18}F]FDG PET/CT to detect recurrence of ER+ BC, in case management depends on the extent of the disease.

It was agreed that wbMR is an option when there is a high suspicion of recurrence, but all other examinations were negative.

4.11.2. Consensus to disagree and no consensus

Similar to track 3, due to the lack of scientific evidence, panellists disagreed with statement n° 83 ("Whenever available, PET/CT with [^{89}Zr]anti-PD1/PD-L1 is preferred to [^{18}F]FDG PET/CT to detect recurrence of triple negative BC") and did not reach consensus on statement n° 82 ("Whenever available, PET/CT with [^{89}Zr]trastuzumab is preferred to [^{18}F]FDG PET/CT to detect recurrence of HER2-positive BC").

4.12. Track 5 – Future Imaging Challenges & Developments in Breast Cancer

Track 5 was composed 7 statements and all were scored as consensus to agree (Table 10).

4.12.1. Consensus to agree

Metabolic parameters (mainly SUVmax, metabolic tumour volume (MTV) and total lesion glycolosis (TLG)) in the primary tumour determined by [^{18}F]FDG PET/CT have prognostic value regarding the outcome, although they are not validated predictive biomarkers. Artificial intelligence (AI)-based software has shown promising results, but AI tools are not yet validated for clinical use.

Structured reporting of [^{18}F]FDG and [^{18}F]FES PET/CT and harmonisation of interpretation criteria should be used in clinical practice, but effective templates and criteria are currently lacking and should be developed.

Although promising data about FAPI-based PET imaging in staging or restaging of patients with lobular breast cancer have been published, further validation is still necessary before clinical implementation. [118, 119] [ref]

Bone targeting radionuclide therapy (e.g. Samarium-153-Lexidronam) is safe and effective in bone pain palliation and can be performed in an outpatient clinic according to local regulations. Further research on bone pain palliation is needed to add to the results from a phase 2 trial with Radium-223 (NCT02366130). [120].

Currently, there are not enough data to support theranostics in breast cancer. Many studies have shown the promising role of several new radiopharmaceuticals in breast cancer, many with theranostics possibility (ex. anti-PD1/PD-L1, FAPI, Bombesin/Gastrin-Releasing Peptide Receptor (GRPR) Antagonist, poly (ADP-ribose) polymerase (PARP), somatostatin receptors (SSTR), insulin-like growth factor-1 (IGF-1R), NECTIN-4, etc.). Among these, FAPI presents reliable and intense uptake in breast cancer and has promising potential for regional nodal and distant disease staging, particularly in lobular cancer [121] and clinical trials are ongoing (ex. LuMIERE: NCT04939610). Furthermore, GRPr/Bombesin also seems to be a promising theranostic target, and the

Table 8
Complementary information about Track 3.

Complementary information about Track 3
• Methods to assess response must be readily available in decentralised institutions, inexpensive, and represent low patient burden.
• [^{18}F]FDG PET/CT may be the preferred modality, whenever possible, over CT and bone scan, to assess systemic response to therapy.
• In countries with breast cancer screening, future efforts will focus on de-escalated treatment approaches, with early efficacy read-outs to avoid overtreatment. PET/CT may play an important role if trials similar to PHERGain are promoted.
• Despite [^{18}F]FDG PET/CT already being used to assess therapy response, oncologists may not be ready to use it routinely. Despite the increasing evidence, current gaps in translating [^{18}F]FDG PET for response assessment towards the clinic still include: selecting patients that benefit most from [^{18}F]FDG PET evaluation, optimal timing to repeat [^{18}F]FDG PET (or adapt timing according to treatment), number of lesions and adequate semiquantitative parameters to be assessed, significance of heterogeneous response, and impact of early response assessment on outcome (mainly toxicities, survival, and quality of life).
• It is necessary to join forces to perform prospective and multicentric trials. Considering that pharmaceutical companies may not be interested in funding trials to assess early response that could lead to treatment interruption, these clinical trials are mainly an academic initiative to benefit patients and healthcare costs.

Table 9
Track 4 Delphi results.

Statement	Median	30th Percentile	70th Percentile	Percent choosing 7, 8, or 9	Interpretation	N choosing unable to score
76. [^{18}F]FDG PET/CT is recommended whenever there is clinical, laboratorial or imaging suspicious of recurrence.	8.5	7	9	96 %	Consensus agree	0
77. When there is suspicion of CNS recurrence, brain MR is the first line imaging modality.	9	9	9	100 %	Consensus agree	0
78. [^{18}F]FDG PET/CT should be used to confirm oligometastatic disease.	9	9	9	96 %	Consensus agree	0
79. [^{18}F]FDG PET/CT is one of the preferred modalities for radiation therapy planning in oligometastatic disease.	9	8	9	88 %	Consensus agree	0
80. Since [^{18}F]FDG PET may not show the total tumour burden in brain and liver due to the physiologic high [^{18}F]FDG uptake, additional organ-targeted MR should be performed to evaluate the full disease extent in the organ.	9	9	9	92 %	Consensus agree	0
81. [^{18}F]FES PET/CT may be considered to complement [^{18}F]FDG PET/CT to detect recurrence of ER+ BC, in case management depends on the extent of the disease.	8	7	8	74 %	Consensus agree	1
82. Whenever available, PET/CT with [^{89}Zr]trastuzumab is preferred to [^{18}F]FDG PET/CT to detect recurrence of HER2-positive BC.	3	1	5.8	30 %	No consensus	1
83. Whenever available, PET/CT with [^{89}Zr]anti-PD1/PD-L1 is preferred to [^{18}F]FDG PET/CT to detect recurrence of triple negative BC.	3	1	5	22 %	Consensus disagree	1
84. wbMR is an option when there is a high suspicion of recurrence, but all other examinations were negative.	7.5	5	8	59 %	Consensus agree	2

Table 10
Track 5 Delphi results.

Statement	Median	30th Pcentile	70th Pcentile	Percent choosing 7, 8, or 9	Interpretation	N choosing unable to score
86. Artificial intelligence-based software are NOT yet validated for clinical characterisation of PET lesions.	9	8	9	87 %	Consensus agree	0
87. Structured reporting of [^{18}F]FDG and [^{18}F]FES PET/CT and harmonisation of interpretation criteria should be used in clinical practice, but effective templates and criteria are currently lacking and should be developed.	9	8	9	100 %	Consensus agree	0
88. FAPI-based PET imaging may be preferred to [^{18}F]FDG PET/CT in staging or restaging of patients with lobular breast cancer.	7	5	7	92 %	Consensus agree	4
89. Bone targeting radionuclide therapy (e.g. Samarium-153-Lexidronam) is safe and effective in bone pain palliation.	7	9	7.9	65 %	Consensus agree	6
90. Bone pain palliation with radiopharmaceuticals can be performed in an outpatient clinic, according to local regulators.	7	9	9	89 %	Consensus agree	5
91. Further research on bone pain palliation is needed, particularly with Radium-223.	8	9	8	95 %	Consensus agree	1
92. Currently, there is not enough data to support extra-bone theranostics in breast cancer (ex. Pembrolizumab, FAPI).	9	9	9	88 %	Consensus agree	0

first clinical trial is ongoing (NeoRay: NCT03872778).

The main topics additionally discussed during Track 5 is presented in Table 11.

5. Conclusions

The EANM Focus Meeting 6 is the first comprehensive multidisciplinary consensus initiative addressing the most relevant settings of breast cancer care, including patient advocacy and imaging as a whole (represented by nuclear medicine and radiology) and is endorsed by key stakeholder organisations: ESSO, EUSOBI, ESTRO and Europa Donna. Overall agreement was achieved in 91 % of the statements, illustrating the most relevant clinical scenarios in breast cancer. Current gaps and future action points were identified. Key opinion leaders and experienced research leads were included, which is essential for raising awareness in the imaging and clinical communities on research

Table 11
Complementary information about Track 5.

Complementary information about Track 5
• Patient-centred care emphasises the importance of the individual in health care with the motto “Nothing about me without me!”, [122] which should be in the minds of all health care professionals. Providing information will engage more patients in their diagnosis and treatment process. Patients prefer to be involved in clinical trials at the design stage, not only as participants.
• The revolution of immunoconjugates for treating cancer represents a major health achievement, and breast cancer is at the forefront with yearly increases in approvals, either new compounds or new indications. Currently, antibody-drug conjugates (ADCs) are the prototypical immunoconjugates for clinical practice, and it is an evolving landscape. [123,124] Some targets and the respective drugs that achieved good results were nominated: (1) HER2: Trastuzumab Emtansine (T-DM1) and Trastuzumab Deruxtecan (T-Dxd); (2) TROP2: Sacituzumab Govitecan, Datopotamab Deruxtecan and Sacituzumab Tirumotecan; (3) HER3: Patritumab-Deruxtecan (HER3-DXd).
• PET in radiation therapy impacts patient selection, contouring, and volume definition. The incorporation of biological/molecular imaging to guide radiation treatment (biology guided radiotherapy) [125] improves radiation planning and therapeutic ratio, through better selective dose delivery. PET-linear accelerator combines these techniques by using radiotracers to deliver biology guided RT. For this, multidisciplinary cooperation is fundamental.

priorities, the design of which may be improved by clinical and imaging cooperation to develop joint initiatives to solve complex problems.

CRediT authorship contribution statement

Sofia Carrilho Vaz: Writing – original draft, Investigation, Data curation, Conceptualization. **Steven MacLennan:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Thiemo van Nijnatten:** Writing – review & editing. **Antoinette Attard:** Writing – review & editing. **Philipp Backhaus:** Writing – review & editing. **Pascal Baltzer:** Writing – review & editing. **Martina Bašić Koretić:** Writing – review & editing. **Tessa Buckle:** Writing – review & editing. **Gary Cook:** Writing – review & editing. **Elizabeth H. Dibble:** Writing – review & editing. **Geraldine Gebhart:** Writing – review & editing. **Alessandra Gennari:** Writing – review & editing. **David Groheux:** Writing – review & editing. **Nadia Harbeck:** Writing – review & editing. **Malene Grubbe Hildebrandt:** Writing – review & editing. **Ritse Mann:** Writing – review & editing. **Frederique Penault-Llorca:** Writing – review & editing. **Katja Pinker:** Writing – review & editing. **Joana M. Ribeiro:** Writing – review & editing. **Sofia Rivera:** Writing – review & editing. **Valeria Romeo:** Writing – review & editing. **Isabel T. Rubio:** Writing – review & editing. **Francesco Schettini:** Writing – review & editing. **Carolien Schroder:** Writing – review & editing. **Giorgio Treglia:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation. **Gary A. Ulaner:** Writing – review & editing. **Michel van Kruchten:** Writing – review & editing. **Wolfgang A. Weber:** Writing – review & editing. **Fatima Cardoso:** Writing – review & editing, Conceptualization. **Karolien Goffin:** Writing – review & editing, Supervision, Conceptualization. **Paola Anna Erba:** Writing – review & editing, Supervision, Conceptualization, Funding acquisition.

Study methodology

Evidence and consensus-based guideline statements.

Ethical standards

For studies involving human participants or human data.

Existing evidence quality was summarised in a systematic search and screen process and assessed using a quality appraisal tool (AMSTAR2). Anonymised expert opinions were gathered via surveys. The need for written informed consent was waived due to the nature of the study.

Ethical standards

For studies involving animal data.

Not applicable.

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Declaration of competing interest

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Appendix A. Supplementary data

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Abbreviations

-ADC - antibody-drug conjugates
-ALND – axillary lymph node dissection
-CSF - cerebrospinal fluid
-CNS – central nervous system
-CT – computerised tomography
-CTCs - circulating tumour cells
-DCIS - ductal carcinoma in situ
-DBT - digital breast tomosynthesis
-ctDNA – circulating tumour DNA
-EANM – European association of nuclear medicine
-ER-positive – estrogen receptors positive
-[18F]FDG – fluoride-18 fluorodeoxyglucose
-[18F]FES – fluoride-18 fluoroestradiol
- HER2-positive - human epidermal receptor type 2
- SBS – sestamibi breast scintigraphy (or other lipophilic cations)
-MG - mammography
-MR - magnetic resonance
-NAST – neoadjuvant systemic therapy

-NST – no special type
-PD-1/L1 – programmed death 1/ligand-1
-PERCIST - Positron Emission Tomography Response Criteria in Solid Tumours
-PET – positron emission tomography
-RECIST - Response Evaluation Criteria in Solid Tumours
-SNMMI – Society of Nuclear Medicine and Molecular Imaging
-SLNB – sentinel lymph node biopsy-US - ultrasonography

Data availability

Data will be made available on request.

References

[1] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2024;74:229–63. https://doi.org/10.3322/CAAC.21834.

[2] Arnold M, Morgan E, Rumgay H, Mafra A, Singh D, Laversanne M, et al. Current and future burden of breast cancer: global statistics for 2020 and 2040. Breast 2022;66:15–23. https://doi.org/10.1016/J.BREAST.2022.08.010.

[3] Lüönd F, Tiede S, Christofori G. Breast cancer as an example of tumour heterogeneity and tumour cell plasticity during malignant progression. Br J Cancer 2021;125:164–75. https://doi.org/10.1038/S41416-021-01328-7.

[4] Mohammed AA. The clinical behavior of different molecular subtypes of breast cancer. Cancer Treat Res Commun 2021;29. https://doi.org/10.1016/J.CTARC.2021.100469.

[5] Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. The Eighth Edition AJCC Cancer Staging Manual: continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin 2017;67:93–9. https://doi.org/10.3322/CAAC.21388.

[6] Groheux D, Vaz SC, De Geus-Oei LF, Dibble EH, Ulaner GA, Cook GJR, et al. 18F-Labeled fluorodeoxyglucose-positron emission tomography/computed tomography in staging and restaging patients with breast cancer. J Clin Oncol 2025. https://doi.org/10.1200/JCO-24-01945.

[7] Palinkas LA, Horwitz SM, Green CA, Wisdom JP, Duan N, Hoagwood K. Purposeful sampling for qualitative data collection and analysis in mixed method implementation research. Adm Policy Ment Health 2015;42:533. https://doi.org/10.1007/S10488-013-0528-Y.

[8] Barrett D, Heale R. What are Delphi studies? Evid Based Nurs 2020;23:68–9. https://doi.org/10.1136/EBNURS-2020-103303.

[9] Niederberger M, Spranger J. Delphi technique in health sciences: a map. Front Public Health 2020;8. https://doi.org/10.3389/FPUBH.2020.00457.

[10] Nasa P, Jain R, Juneja D. Delphi methodology in healthcare research: how to decide its appropriateness. World J Methodol 2021;11:116. https://doi.org/10.5662/WJM.V11.I4.116.

[11] Niederberger M, Schifano J, Deckert S, Hirt J, Homberg A, Köberich S, et al. Delphi studies in social and health sciences—recommendations for an interdisciplinary standardized reporting (DELPHISTAR). Results of a Delphi study. PLoS One 2024;19:e0304651. https://doi.org/10.1371/JOURNAL.PONE.0304651.

[12] Decision Eyes (company). Welphi 2025.

[13] Kathryn Fitch, Bernstein Steven, Aguilar MDolores, Bernard Burnand, JRamon LaCalle, Pablo Lazaro, et al. The Rand/UCLA appropriateness method user's manual. Rand; 2001.

[14] Microsoft Corporation. Microsoft excel. Retrieved from, https://office.microsoft.com/excel; 2018 [n.d.].

[15] Boellaard R, Delgado-Bolton R, Oyen WJG, Giammarile F, Tatsch K, Eschner W, et al. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. Eur J Nucl Med Mol Imaging 2015;42:328–54. https://doi.org/10.1007/S00259-014-2961-X.

[16] Vaz SC, Woll JPP, Cardoso F, Groheux D, Cook GJR, Ulaner GA, et al. Joint EANM-SNMMI guideline on the role of 2-[18F]FDG PET/CT in no special type breast cancer : (endorsed by the ACR, ESSO, ESTRO, EUSOBI/ESR, and EUSOMA). Eur J Nucl Med Mol Imaging 2024;51:2706–32. https://doi.org/10.1007/S00259-024-06696-9.

[17] Mankoff D, Balogova S, Dunnwald L, Dehdashti F, DeVries E, Evangelista L, et al. Summary: SNMMI procedure standard/EANM practice guideline for estrogen receptor imaging of patients with breast cancer using 16α-[18F]Fluoro-17β-Estradiol PET. J Nucl Med 2024;65:221–3. https://doi.org/10.2967/JNUMED.123.266938.

[18] Ulaner GA. 16α-18F-fluoro-17β-Fluoroestradiol (FES): clinical applications for patients with breast cancer. Semin Nucl Med 2022;52:574–83. https://doi.org/10.1053/J.SEMNUCLMED.2022.03.002.

[19] van Es SC, Velleman T, Elias SG, Bensch F, Brouwers AH, Glaudemans AWJM, et al. Assessment of bone lesions with 18F-FDG PET compared with 99mTc bone scintigraphy leads to clinically relevant differences in metastatic breast cancer management. J Nucl Med 2021;62:177–83. https://doi.org/10.2967/JNUMED.120.244640.

[20] Spadafora M, De Rimini ML, Catalano M, Lastoria S, Squame F, Falzarano M, et al. Regulatory and clinical implications of using diagnostic CT in PET/CT. Clin Transl Imaging 2025;13:275–81. https://doi.org/10.1007/S40336-025-00700-4/TABLES/3.

[21] Kaalep A, Sera T, Oyen W, Krause BJ, Chiti A, Liu Y, et al. EANM/EARL FDG-PET/CT accreditation - summary results from the first 200 accredited imaging systems. Eur J Nucl Med Mol Imaging 2018;45:412–22. https://doi.org/10.1007/S00259-017-3853-7.

[22] Aide N, Lasnon C, Veit-Haibach P, Sera T, Sattler B, Boellaard R. EANM/EARL harmonization strategies in PET quantification: from daily practice to multicentre oncological studies. Eur J Nucl Med Mol Imaging 2017;44:17–31. https://doi.org/10.1007/S00259-017-3740-2.

[23] Roya M, van Snick JH, Slart RHJA, Noordzij W, Stormezand GN, Willemsen ATM, et al. Clinical performance comparison of a long versus a short axial field-of-view PET/CT using EARL-compliant reconstructions. Mol Imaging Biol 2024;26. https://doi.org/10.1007/S11307-024-01939-5.

[24] American College of Radiology ACR Appropriateness Criteria ® Breast imaging during pregnancy [n.d].

[25] Bookwalter CA, McDonald RJ, Packard AT, Little JT, McDonald JS, Watson RobertE, et al. Contrast Media in Pregnant and Lactating Patients, From the AJR Special Series on Contrast Media. Https://WwwAjronlineOrg/2024. https://doi.org/10.2214/AJR.24.31415.

[26] ESUR GUIDELINES ON CONTRAST AGENTS | esur.org n.d. https://www.esur.org/esur-guidelines-on-contrast-agents/(accessed July 31, 2025).

[27] Burton CS, Frey K, Fahey F, Kaminski MS, Brown RKJ, Pohlen JM, et al. Fetal dose from PET and CT in pregnant patients. J Nucl Med 2023;64:312–9. https://doi.org/10.2967/JNUMED.122.263959.

[28] Smith CLC, Yaqub M, Wellenberg RHH, Knip JJ, Boellaard R, Zwezerijnen GJC. Ultra-low foetal radiation exposure in 18F-FDG PET/CT imaging with a long axial field-of-view PET/CT system. EJNMMI Phys 2024;11. https://doi.org/10.1186/S40658-024-00648-W.

[29] Zanotti-Fregonara P, Ishiguro T, Yoshihara K, Ishii S, Enomoto T. 18F-FDG fetal dosimetry calculated with PET/MRI. J Nucl Med 2022;63:1592–7. https://doi.org/10.2967/JNUMED.121.263561.

[30] van Nijnatten TJA, de Mooij CM, Mitea C, Houwers J, de Boer M, Smidt ML, et al. [18F]FDG whole-body PET-MR including an integrated breast MR protocol for locoregional and distant staging in breast cancer patients-a feasibility study. Insights Imaging 2024;15:243. https://doi.org/10.1186/S13244-024-01830-5.

[31] Gradishar WJ, Moran MS, Abraham J, Aft R, Agnese D, Allison KH, et al. Breast cancer, version 3.2022, NCCN clinical practice guidelines in oncology. J Natl Compr Cancer Netw 2022;20:691–722. https://doi.org/10.6004/JNCCN.2022.0030.

[32] Loibl S, André F, Bachelot T, Barrios CH, Bergh J, Burstein HJ, et al. Early breast cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol 2024;35:159–82. https://doi.org/10.1016/j.annonc.2023.11.016.

[33] Hruska CB, Corion C, Geus-Oei L-F de, Adrada BE, Fowler AM, Hunt KN, et al. SNMMI procedure standard/EANM practice guideline for molecular breast imaging with dedicated γ-cameras. J Nucl Med Technol 2022;50:103–10. https://doi.org/10.2967/JNMT.121.264204.

[34] Dibble EH, Vaz SCarrillo, Banu Arun, Fowler Amy, Geus-Oei L-F de, Hunt Katie, et al. Appropriate use criteria for molecular breast imaging in gamma-cameras. J Nucl Med Technol 2025. In press.

[35] Evans A, Trimboli RM, Athanasiou A, Balleyguier C, Baltzer PA, Bick U, et al. Breast ultrasound: recommendations for information to women and referring physicians by the European Society of Breast Imaging. Insights Imaging 2018;9:449–61. https://doi.org/10.1007/S13244-018-0636-Z.

[36] Gentilini OD, Botteri E, Sangalli C, Galimberti V, Porpiglia M, Agresti R, et al. Sentinel lymph node biopsy vs No axillary surgery in patients with small breast cancer and negative results on ultrasonography of axillary lymph nodes: the SOUND randomized clinical trial. JAMA Oncol 2023;9:1557–64. https://doi.org/10.1001/JAMAONCOL.2023.3759.

[37] Reimer T, Stachs A, Veselinovic K, Kühn T, Heil J, Polata S, et al. Axillary surgery in breast cancer - primary results of the INSEMA trial. N Engl J Med 2024. https://doi.org/10.1056/NEJMOA2412063.

[38] van Roozendaal LM, Vane MLG, van Dalen T, Hage JA, Strobbe LJA, Boersma LJ, et al. Clinically node negative breast cancer patients undergoing breast conserving therapy, sentinel lymph node procedure versus follow-up: a Dutch randomized controlled multicentre trial (BOOG 2013-08). BMC Cancer 2017;17. https://doi.org/10.1186/S12885-017-3443-X.

[39] Jung JG, Ahn SH, Lee S, Kim EK, Ryu JM, Park S, et al. No axillary surgical treatment for lymph node-negative patients after ultra-sonography [NAUTILUS]: protocol of a prospective randomized clinical trial. BMC Cancer 2022;22. https://doi.org/10.1186/S12885-022-09273-1.

[40] van Nijnatten TJA, Poplack SP, Wijgers RA, Kilburn-Toppin F, Athanasiou A, Chang JM, et al. Differences in axillary ultrasound protocols among prospective de-escalating axillary surgical staging trials in clinically node negative early breast cancer patients. Eur J Radiol 2024;181. https://doi.org/10.1016/j.ejrad.2024.111775.

[41] Giammarile F, Vidal-Sicart S, Paez D, Pellet O, Enrique EL, Mikhail-Lette M, et al. Sentinel lymph node methods in breast cancer. Semin Nucl Med 2022;52:551–60. https://doi.org/10.1053/J.SEMNUCLMED.2022.01.006.

[42] Riedl CC, Slobod E, Jochelson M, Morrow M, Goldman DA, Gonen M, et al. Retrospective analysis of 18F-FDG PET/CT for staging asymptomatic breast cancer patients younger than 40 years. J Nucl Med 2014;55:1578–83. https://doi.org/10.2967/JNUMED.114.143297.

[43] Ulaner GA, Castillo R, Goldman DA, Wills J, Riedl CC, Pinker-Domenig K, et al. 18F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast

cancer. Eur J Nucl Med Mol Imaging 2016;43:1937–44. https://doi.org/10.1007/S00259-016-3402-9.
[44] Giuliano AE, McCall L, Beitsch P, Whitworth PW, Blumencranz P, Leitch AM, et al. Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: the American College of Surgeons Oncology Group Z0011 randomized trial. Ann Surg 2010;252:426–32. https://doi.org/10.1097/SLA.0B013E3181F08F32.
[45] Giuliano AE, Ballman KV, McCall L, Beitsch PD, Brennan MB, Kelemen PR, et al. Effect of axillary dissection vs No axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: the ACOSOG Z0011 (Alliance) randomized clinical trial. JAMA 2017;318:918–26. https://doi.org/10.1001/JAMA.2017.11470.
[46] Hersh EH, King TA. De-escalating axillary surgery in early-stage breast cancer. Breast 2022;62(Suppl 1):S43–9. https://doi.org/10.1016/J.BREAST.2021.11.018.
[47] Montagna G, Mrdutt MM, Sun SX, Hlavin C, Diego EJ, Wong SM, et al. Omission of axillary dissection following nodal downstaging with neoadjuvant chemotherapy. JAMA Oncol 2024;10. https://doi.org/10.1001/JAMAONCOL.2024.0578.
[48] Boughey JC, Yu H, Dugan CL, Piltin MA, Postlewait L, Son JD, et al. Changes in surgical management of the axilla over 11 Years - report on more than 1500 breast cancer patients treated with neoadjuvant chemotherapy on the prospective I-SPY2 trial. Ann Surg Oncol 2023;30:6401–10. https://doi.org/10.1245/S10434-023-13759-Y.
[49] Alamoodi M, Wazir U, Mokbel K, Patani N, Varghese J, Mokbel K. Omitting sentinel lymph node biopsy after neoadjuvant systemic therapy for clinically node negative HER2 positive and triple negative breast cancer: a pooled analysis. Cancers (Basel) 2023;15. https://doi.org/10.3390/CANCERS15133325.
[50] Ryu JM, Lee H, Han W, Lee HB, Ahn SG, Kim HJ, et al. Selective avoidance of sentinel lymph node biopsy after neoadjuvant chemotherapy in human epidermal growth factor 2-positive/triple-negative breast cancer patients with excellent response. J Breast Cancer 2024;27:130–40. https://doi.org/10.4048/JBC.2023.0264.
[51] Reimer T. Omission of axillary sentinel lymph node biopsy in early invasive breast cancer. Breast 2023;67:124–8. https://doi.org/10.1016/J.BREAST.2023.01.002.
[52] Gentilini OD, Botteri E, Sangalli C, Galimberti V, Porpiglia M, Agresti R, et al. Sentinel lymph node biopsy vs No axillary surgery in patients with small breast cancer and negative results on ultrasonography of axillary lymph nodes: the SOUND randomized clinical trial. JAMA Oncol 2023;9:1557–64. https://doi.org/10.1001/JAMAONCOL.2023.3759.
[53] Reimer T, Stachs A, Veselinovic K, Kühn T, Heil J, Polata S, et al. Axillary surgery in breast cancer - primary results of the INSEMA trial. N Engl J Med 2024. https://doi.org/10.1056/NEJMOA2412063.
[54] Giuliano AE, Connolly JL, Edge SB, Mittendorf EA, Rugo HS, Solin LJ, et al. Breast Cancer-Major changes in the American Joint Committee on Cancer eighth edition cancer staging manual. CA Cancer J Clin 2017;67:290–303. https://doi.org/10.3322/CAAC.21393.
[55] Groheux D, Hindié E, Delord M, Giacchetti S, Hamy AS, De Bazelaire C, et al. Prognostic impact of (18)FDG-PET-CT findings in clinical stage III and IIB breast cancer. J Natl Cancer Inst 2012;104:1879–87. https://doi.org/10.1093/JNCI/DJS451.
[56] Dayes IS, Metser U, Hodgson N, Parpia S, Eisen AF, George R, et al. Impact of 18F-labeled fluorodeoxyglucose positron emission tomography-computed tomography versus conventional staging in patients with locally advanced breast cancer. J Clin Oncol 2023;41:3909–16. https://doi.org/10.1200/JCO.23.00249.
[57] Ko H, Baghdadi Y, Love C, Sparano JA. Clinical utility of 18F-FDG PET/CT in staging localized breast cancer before initiating preoperative systemic therapy. J Natl Compr Canc Netw 2020;18:1240–6. https://doi.org/10.6004/JNCCN.2020.7592.
[58] Groheux D, Vaz SC, Poortmans P, Mann RM, Ulaner GA, Cook GJR, et al. Role of [18F]FDG PET/CT in patients with invasive breast carcinoma of no special type: literature review and comparison between guidelines. Breast 2024;78. https://doi.org/10.1016/J.BREAST.2024.103806.
[59] Cardoso F, Paluch-Shimon S, Schumacher-Wulf E, Matos L, Gelmon K, Aapro MS, et al. 6th and 7th International consensus guidelines for the management of advanced breast cancer (ABC guidelines 6 and 7). Breast : Official Journal of the European Society of Mastology 2024;76:103756. https://doi.org/10.1016/J.BREAST.2024.103756.
[60] Gennari A, André F, Barrios CH, Cortés J, de Azambuja E, DeMichele A, et al. ESMO Clinical Practice Guideline for the diagnosis, staging and treatment of patients with metastatic breast cancer. Ann Oncol 2021;32:1475–95. https://doi.org/10.1016/j.annonc.2021.09.019.
[61] Lin CY, Lin CL, Kao CH. Staging/restaging performance of F18-fluorodeoxyglucose positron emission tomography/magnetic resonance imaging in breast cancer: a review and meta-analysis. Eur J Radiol 2018;107:158–65. https://doi.org/10.1016/J.EJRAD.2018.09.003.
[62] Romeo V, Helbich TH, Pinker K. Breast PET/MRI hybrid imaging and targeted tracers. J Magn Reson Imaging 2023;57:370–86. https://doi.org/10.1002/JMRI.28431.
[63] Van Geel JJL, Boers J, Elias SG, Glaudemans AWJM, De Vries EFJ, Hospers GAP, et al. Clinical validity of 16α-[18F]Fluoro-17β-Estradiol positron emission tomography/computed tomography to assess estrogen receptor status in newly diagnosed metastatic breast cancer. J Clin Oncol 2022;40. https://doi.org/10.1200/JCO.22.00400.
[64] Gennari A, Brain E, De Censi A, Nanni O, Wuerstlein R, Frassoldati A, et al. Early prediction of endocrine responsiveness in ER+/HER2-negative metastatic breast cancer (MBC): pilot study with 18F-fluoroestradiol (18F-FES) CT/PET. Ann Oncol 2024;35:549–58. https://doi.org/10.1016/J.ANNONC.2024.02.007.
[65] Ulaner GA, Mankoff DA, Clark AS, Fowler AM, Linden HM, Peterson LM, et al. Summary: appropriate use criteria for estrogen receptor-targeted PET imaging with 16α-18F-Fluoro-17β-Fluoroestradiol. J Nucl Med 2023;64:351–4. https://doi.org/10.2967/JNUMED.123.265420.
[66] Parihar AS, Vaz S, Sutcliffe S, Pant N, Schoones JW, Ulaner GA. 18F-Fluoroestradiol PET/CT for predicting benefit from endocrine therapy in patients with estrogen receptor-positive breast cancer: a systematic review and metaanalysis. J Nucl Med 2025;124:269163. https://doi.org/10.2967/JNUMED.124.269163. jnumed.
[67] Boers J, Eisses B, Zwager MC, van Geel JJL, Bensch F, de Vries EFJ, et al. Correlation between histopathological prognostic tumor characteristics and [18F]FDG uptake in corresponding metastases in newly diagnosed metastatic breast cancer. Diagnostics 2024;14. https://doi.org/10.3390/DIAGNOSTICS14040416.
[68] Moustaquim J. Comparative analysis of [18F]FES- and [18F]FDG-PET in patients with metastatic ER+ lobular breast cancer. San Antonio Breast Cancer Symposium 2024.
[69] Eisses B, van Geel JJL, Brouwers AH, Bensch F, Elias SG, Kuip EJM, et al. Whole-body HER2 heterogeneity identified on HER2 PET in HER2-negative, -low, and -positive metastatic breast cancer. J Nucl Med 2024;65:267636. https://doi.org/10.2967/JNUMED.124.267636. jnumed.124.
[70] Mileva M, de Vries EGE, Guiot T, Wimana Z, Deleu AL, Schröder CP, et al. Molecular imaging predicts lack of T-DM1 response in advanced HER2-positive breast cancer (final results of ZEPHIR trial). NPJ Breast Cancer 2024;10. https://doi.org/10.1038/S41523-023-00610-6.
[71] Gebhart G, Lamberts LE, Wimana Z, Garcia C, Emonts P, Ameye L, et al. Molecular imaging as a tool to investigate heterogeneity of advanced HER2-positive breast cancer and to predict patient outcome under trastuzumab emtansine (T-DM1): the ZEPHIR trial. Ann Oncol 2016;27:619–24. https://doi.org/10.1093/ANNONC/MDV577.
[72] Altena R, Burén S, Blomgren A, Karlsson E, Tzortzakakis A, Brun N, et al. Human epidermal growth factor receptor 2 (HER2) PET imaging of HER2-low breast cancer with [68Ga]Ga-ABY-025: results from a pilot study. J Nucl Med 2024;65:700–7. https://doi.org/10.2967/JNUMED.123.266847.
[73] Xavier C, Vaneycken I, D'Huyvetter M, Heemskerk J, Keyaerts M, Vincke C, et al. Synthesis, preclinical validation, dosimetry, and toxicity of 68Ga-NOTA-anti-HER2 Nanobodies for iPET imaging of HER2 receptor expression in cancer. J Nucl Med 2013;54:776–84. https://doi.org/10.2967/JNUMED.112.111021.
[74] Keyaerts M, Xavier C, Heemskerk J, Devoogdt N, Everaert H, Ackaert C, et al. Phase I study of 68Ga-HER2-Nanobody for PET/CT assessment of HER2 expression in breast carcinoma. J Nucl Med 2016;57:27–33. https://doi.org/10.2967/JNUMED.115.162024.
[75] Altunay B, Morgenroth A, Beheshti M, Vogg A, Wong NCL, Ting HH, et al. HER2-directed antibodies, affibodies and nanobodies as drug-delivery vehicles in breast cancer with a specific focus on radioimmunotherapy and radioimmunoimaging. Eur J Nucl Med Mol Imaging 2021;48:1371–89. https://doi.org/10.1007/S00259-020-05094-1.
[76] Bensch F, van der Veen EL, Lub-de Hooge MN, Jorritsma-Smit A, Boellaard R, Kok IC, et al. 89Zr-atezolizumab imaging as a non-invasive approach to assess clinical response to PD-L1 blockade in cancer. Nat Med 2018;24:1852–8. https://doi.org/10.1038/S41591-018-0255-8.
[77] Schwartz LH, Litière S, De Vries E, Ford R, Gwyther S, Mandrekar S, et al. RECIST 1.1 - update and clarification: from the RECIST committee. Eur J Cancer 2016;62:132–7. https://doi.org/10.1016/j.ejca.2016.03.081.
[78] Vogsen M, Harbo F, Jakobsen NM, Nissen HJ, Dahlsgaard-Wallenius SE, Gerke O, et al. Response monitoring in metastatic breast cancer: a prospective study comparing 18F-FDG PET/CT with conventional CT. J Nucl Med 2023;64:355–61. https://doi.org/10.2967/JNUMED.121.263358.
[79] Vaz SC, Groheux D, van Nijnatten T, Antunovic L, Cardoso F, Mottaghy F, et al. Editorial Commentary: should "heterogeneous response" be considered as new category for assessing treatment response in patients with breast cancer? Eur J Nucl Med Mol Imaging 2025;52. https://doi.org/10.1007/S00259-024-07042-9.
[80] Joo Hyun O, Lodge MA, Wahl RL. Practical PERCIST: a simplified guide to PET response criteria in solid tumors 1.0. Radiology 2016;280:576–84. https://doi.org/10.1148/RADIOL.2016142043.
[81] Pinker K, Riedl C, Weber WA. Evaluating tumor response with FDG PET: updates on PERCIST, comparison with EORTC criteria and clues to future developments. Eur J Nucl Med Mol Imaging 2017;44:55–66. https://doi.org/10.1007/S00259-017-3687-3.
[82] Wahl RL, Jacene H, Kasamon Y, Lodge MA. From RECIST to PERCIST: evolving Considerations for PET response criteria in solid tumors. J Nucl Med 2009;50(Suppl 1). https://doi.org/10.2967/JNUMED.108.057307.
[83] Lopci E, Hicks RJ, Dimitrakopoulou-Strauss A, Dercle L, Iravani A, Seban RD, et al. Joint EANM/SNMMI/ANZSNM practice guidelines/procedure standards on recommended use of [18F]FDG PET/CT imaging during immunomodulatory treatments in patients with solid tumors version 1.0. Eur J Nucl Med Mol Imaging 2022;49:2323–41. https://doi.org/10.1007/S00259-022-05780-2.
[84] Gerke O, Naghavi-Behzad M, Nygaard ST, Sigaroudi VR, Vogsen M, Vach W, et al. Diagnosing bone metastases in breast cancer: a systematic review and network meta-analysis on diagnostic test accuracy studies of 2-[18F]FDG-PET/CT, 18F-NaF-PET/CT, MRI, contrast-enhanced CT, and bone scintigraphy. Semin Nucl Med 2025;55. https://doi.org/10.1053/J.SEMNUCLMED.2024.10.008.

[85] van Geel JJL, de Vries EFJ, van Kruchten M, Hospers GAP, Glaudemans AWJM, Schröder CP. Molecular imaging as biomarker for treatment response and outcome in breast cancer. Ther Adv Med Oncol 2023;15. https://doi.org/10.1177/17588359231170738.

[86] Vogsen M, Naghavi-Behzad M, Harbo FG, Jakobsen NM, Gerke O, Asmussen JT, et al. 2-[18F]FDG-PET/CT is a better predictor of survival than conventional CT: a prospective study of response monitoring in metastatic breast cancer. Sci Rep 2023;13. https://doi.org/10.1038/S41598-023-32727-W.

[87] Seale KN, Tkaczuk KHR. Circulating biomarkers in breast cancer. Clin Breast Cancer 2022;22:e319–31. https://doi.org/10.1016/j.clbc.2021.09.006.

[88] Klocker EV, Suppan C. Liquid biopsy in breast cancer. Memo - Magazine of European Medical Oncology 2024;17:194–7. https://doi.org/10.1007/S12254-024-00975-9/METRICS.

[89] Caracciolo M, Castello A, Urso L, Borgia F, Marzola MC, Uccelli L, et al. Comparison of MRI vs. [18F]FDG PET/CT for treatment response evaluation of primary breast cancer after neoadjuvant chemotherapy: literature review and future perspectives. J Clin Med 2023;12. https://doi.org/10.3390/JCM12165355.

[90] Li H, Yao L, Jin P, Hu L, Li X, Guo T, et al. MRI and PET/CT for evaluation of the pathological response to neoadjuvant chemotherapy in breast cancer: a systematic review and meta-analysis. Breast 2018;40:106–15. https://doi.org/10.1016/J.BREAST.2018.04.018.

[91] Tian F, Shen G, Deng Y, Diao W, Jia Z. The accuracy of 18F-FDG PET/CT in predicting the pathological response to neoadjuvant chemotherapy in patients with breast cancer: a meta-analysis and systematic review. Eur Radiol 2017;27:4786–96. https://doi.org/10.1007/S00330-017-4831-Y.

[92] Wang Y, Zhang C, Liu J, Huang G. Is 18F-FDG PET accurate to predict neoadjuvant therapy response in breast cancer? A meta-analysis. Breast Cancer Res Treat 2012;131:357–69. https://doi.org/10.1007/S10549-011-1780-Z.

[93] Han S, Choi JY. Prognostic value of 18F-FDG PET and PET/CT for assessment of treatment response to neoadjuvant chemotherapy in breast cancer: a systematic review and meta-analysis. Breast Cancer Res 2020;22. https://doi.org/10.1186/S13058-020-01350-2.

[94] Coudert B, Pierga JY, Mouret-Reynier MA, Kerrou K, Ferrero JM, Petit T, et al. Long-term outcomes in patients with PET-predicted poor-responsive HER2-positive breast cancer treated with neoadjuvant bevacizumab added to trastuzumab and docetaxel: 5-year follow-up of the randomised Avataxher study. eClinicalMedicine 2020;28. https://doi.org/10.1016/J.ECLINM.2020.100566.

[95] Pérez-García JM, Cortés J, Ruiz-Borrego M, Colleoni M, Stradella A, Bermejo B, et al. 3-year invasive disease-free survival with chemotherapy de-escalation using an 18F-FDG-PET-based, pathological complete response-adapted strategy in HER2-positive early breast cancer (PHERGain): a randomised, open-label, phase 2 trial. Lancet 2024;403:1649–59. https://doi.org/10.1016/S0140-6736(24)00054-0.

[96] Pérez-García JM, Gebhart G, Ruiz Borrego M, Stradella A, Bermejo B, Schmid P, et al. Chemotherapy de-escalation using an 18F-FDG-PET-based pathological response-adapted strategy in patients with HER2-positive early breast cancer (PHERGain): a multicentre, randomised, open-label, non-comparative, phase 2 trial. Lancet Oncol 2021;22:858–71. https://doi.org/10.1016/S1470-2045(21)00122-4.

[97] van der Voort A, Louis FM, van Ramshorst MS, Kessels R, Mandjes IA, Kemper I, et al. MRI-guided optimisation of neoadjuvant chemotherapy duration in stage II–III HER2-positive breast cancer (TRAIN-3): a multicentre, single-arm, phase 2 study. Lancet Oncol 2024;25:603–13. https://doi.org/10.1016/S1470-2045(24)00104-9.

[98] Helland F, Henriksen MH, Gerke O, Vogsen M, Højlund-Carlsen PF, Grubbe Hildebrandt M. FDG-PET/CT versus contrast-enhanced CT for response evaluation in metastatic breast cancer: a systematic review. Diagnostics 2019;9. https://doi.org/10.3390/DIAGNOSTICS9030106.

[99] Riedl CC, Pinker K, Ulaner GA, Ong LT, Baltzer P, Jochelson MS, et al. Comparison of FDG-PET/CT and contrast-enhanced CT for monitoring therapy response in patients with metastatic breast cancer. Eur J Nucl Med Mol Imaging 2017;44:1428. https://doi.org/10.1007/S00259-017-3703-7.

[100] Naghavi-Behzad M, Vogsen M, Vester RM, Olsen MMB, Oltmann H, Braad PE, et al. Response monitoring in metastatic breast cancer: a comparison of survival times between FDG-PET/CT and CE-CT. Br J Cancer 2022;126:1271–9. https://doi.org/10.1038/S41416-021-01654-W.

[101] Makhlin I, Korhonen KE, Martin ML, Gillman J, Schubert E, Pantel AR, et al. 18F-FDG PET/CT for the evaluation of therapy response in hormone receptor-positive bone-dominant metastatic breast cancer. Radiol Imaging Cancer 2022;4. https://doi.org/10.1148/RYCAN.220032.

[102] Schroder CP, Geel J, Eisses B, Elias SG, Brouwers AH, Bensch F, et al. Clinical utility of molecular imaging in newly diagnosed metastatic breast cancer. J Clin Oncol 2024;42:1019. https://doi.org/10.1200/JCO.2024.42.16_SUPPL.1019.1019.

[103] Lother D, Robert M, Elwood E, Smith S, Tunariu N, Johnston SRD, et al. Imaging in metastatic breast cancer, CT, PET/CT, MRI, WB-DWI, CCA: review and new perspectives. Cancer Imaging 2023;23. https://doi.org/10.1186/S40644-023-00557-8.

[104] Boers J, Venema CM, de Vries EFJ, Glaudemans AWJM, Kwee TC, Schuuring E, et al. Molecular imaging to identify patients with metastatic breast cancer who benefit from endocrine treatment combined with cyclin-dependent kinase inhibition. Eur J Cancer 2020;126:11–20. https://doi.org/10.1016/J.EJCA.2019.10.024.

[105] Liu C, Hu S, Xu X, Zhang Y, Wang B, Song S, et al. Evaluation of tumour heterogeneity by 18F-fluoroestradiol PET as a predictive measure in breast cancer patients receiving palbociclib combined with endocrine treatment. Breast Cancer Res 2022;24. https://doi.org/10.1186/S13058-022-01555-7.

[106] Holleczek B, Stegmaier C, Radosa JC, Solomayer EF, Brenner H. Risk of loco-regional recurrence and distant metastases of patients with invasive breast cancer up to ten years after diagnosis - results from a registry-based study from Germany. BMC Cancer 2019;19. https://doi.org/10.1186/S12885-019-5710-5.

[107] van Maaren MC, de Munck L, Strobbe LJA, Sonke GS, Westenend PJ, Smidt ML, et al. Ten-year recurrence rates for breast cancer subtypes in The Netherlands: a large population-based study. Int J Cancer 2019;144:263–72. https://doi.org/10.1002/IJC.31914.

[108] Grinda T, Joyon N, Lusque A, Lefèvre S, Arnould L, Penault-Llorca F, et al. Phenotypic discordance between primary and metastatic breast cancer in the large-scale real-life multicenter French ESME cohort. NPJ Breast Cancer 2021;7. https://doi.org/10.1038/S41523-021-00252-6.

[109] Lu WL, Jansen L, Post WJ, Bonnema J, Van De Velde JC, De Bock GH. Impact on survival of early detection of isolated breast recurrences after the primary treatment for breast cancer: a meta-analysis. Breast Cancer Res Treat 2009;114:403–12. https://doi.org/10.1007/S10549-008-0023-4.

[110] Schneble EJ, Graham LJ, Shupe MP, Flynt FL, Banks KP, Kirkpatrick AD, et al. Current approaches and Challenges in early detection of breast cancer recurrence. J Cancer 2014;5:281. https://doi.org/10.7150/JCA.8016.

[111] Vogsen M, Jensen JD, Gerke O, Jylling AMB, Asmussen JT, Christensen IY, et al. Benefits and harms of implementing [18F]FDG-PET/CT for diagnosing recurrent breast cancer: a prospective clinical study. EJNMMI Res 2021;11. https://doi.org/10.1186/S13550-021-00833-3.

[112] Piva R, Ticconi F, Ceriani V, Scalorbi F, Fiz F, Capitanio S, et al. Comparative diagnostic accuracy of 18F-FDG PET/CT for breast cancer recurrence. Breast Cancer 2017;9:461–71. https://doi.org/10.2147/BCTT.S111098.

[113] Lee CI, Gold LS, Nelson HD, Chou R, Ramsey SD, Sullivan SD. Comparative effectiveness of imaging modalities to determine metastatic breast cancer treatment response. Breast 2015;24:3–11. https://doi.org/10.1016/J.BREAST.2014.11.009.

[114] Hansen JA, Naghavi-Behzad M, Gerke O, Baun C, Falch K, Duvnjak S, et al. Diagnosis of bone metastases in breast cancer: lesion-based sensitivity of dual-time-point FDG-PET/CT compared to low-dose CT and bone scintigraphy. PLoS One 2021;16. https://doi.org/10.1371/JOURNAL.PONE.0260066.

[115] Pasquier D, Bidaut L, Oprea-Lager DE, deSouza NM, Krug D, Collette L, et al. Designing clinical trials based on modern imaging and metastasis-directed treatments in patients with oligometastatic breast cancer: a consensus recommendation from the EORTC Imaging and Breast Cancer Groups. Lancet Oncol 2023;24:e331–43. https://doi.org/10.1016/S1470-2045(23)00286-3.

[116] Moustaquim J, van Wonderen GE, van Geel JL, van Kruchten M, de Vries EF, Jager A, et al. The impact of staging with [18F]FDG PET/CT or ceCT plus bone scintigraphy on long-term outcomes in metastatic breast cancer: numbers matter. ESMO meeting 2025:2025. Berlin, Germany., Berlin.

[117] De Mooij CM, Sunen I, Mitea C, Lalji UC, Vanwetswinkel S, Smidt ML, et al. Diagnostic performance of PET/computed tomography versus PET/MRI and diffusion-weighted imaging in the N- and M-staging of breast cancer patients. Nucl Med Commun 2020;41:995–1004. https://doi.org/10.1097/MNM.0000000000001254.

[118] Eshet Y, Tau N, Apter S, Nissan N, Levanon K, Bernstein-Molho R, et al. The role of 68Ga-FAPI PET/CT in detection of metastatic lobular breast cancer. Clin Nucl Med 2023;48:228–32. https://doi.org/10.1097/RLU.0000000000004540.

[119] Sahin E, Kus T, Aytekin A, Uzun E, Elboga U, Yilmaz L, et al. 68Ga-FAPI PET/CT as an alternative to 18F-FDG PET/CT in the imaging of invasive lobular breast carcinoma. J Nucl Med 2024;65:512–9. https://doi.org/10.2967/JNUMED.123.266798.

[120] Ueno NT, Tahara RK, Fujii T, Reuben JM, Gao H, Saigal B, et al. Phase II study of Radium-223 dichloride combined with hormonal therapy for hormone receptor-positive, bone-dominant metastatic breast cancer. Cancer Med 2020;9:1025–32. https://doi.org/10.1002/CAM4.2780.

[121] Yadav MP, Ballal S, Martin M, Roesch F, Satapathy S, Moon ES, et al. Therapeutic potential of [177Lu]Lu-DOTAGA-FAPi dimers in metastatic breast cancer patients with limited treatment options: efficacy and safety assessment. Eur J Nucl Med Mol Imaging 2024;51:805–19. https://doi.org/10.1007/S00259-023-06482-Z.

[122] Zelmer J. Nothing about me without me. Healthc Policy 2019;14:6–9. https://doi.org/10.12927/HCPOL.2019.25861.

[123] Tarantino P, Carmagnani Pestana R, Corti C, Modi S, Bardia A, Tolaney SM, et al. Antibody-drug conjugates: smart chemotherapy delivery across tumor histologies. CA Cancer J Clin 2022;72:165–82. https://doi.org/10.3322/CAAC.21705.

[124] Schettini F, Nucera S, Pascual T, Martínez-Sáez O, Sánchez-Bayona R, Conte B, et al. Efficacy and safety of antibody-drug conjugates in pretreated HER2-low metastatic breast cancer: a systematic review and network meta-analysis. Cancer Treat Rev 2025;132:102865. https://doi.org/10.1016/J.CTRV.2024.102865.

[125] Seyedin SN, Gannon MK, Plichta KA, Abushahin L, Berg DJ, Arshava EV, et al. Safety and efficacy of stereotactic body radiation therapy for locoregional recurrences after prior chemoradiation for advanced esophageal carcinoma. Front Oncol 2020;10. https://doi.org/10.3389/FONC.2020.01311.