

# Clinical practice guidelines for sentinel lymph node biopsy in patients with early-stage breast cancer: Chinese Society of Breast Surgery (CSBrS) practice guidelines 2021

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Axillary lymph node assessment is one of the important indicators in the clinical pathological staging of breast cancer. Studies have shown that sentinel lymph node biopsy (SLNB) has the advantages of fewer complications and less trauma than conventional axillary lymph node dissection (ALND).<sup>[1]</sup> Common mapping methods for SLNB include blue dye, radioisotopes, a combination of blue dye and radioisotopes, and fluorescence imaging. To standardize the SLNB techniques for breast cancer, the Chinese Society of Breast Surgery (CSBrS) re-evaluated the quality of evidence for clinical studies of SLNB for breast cancer, referring to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE), and developed the Clinical Practice Guidelines for Sentinel Lymph Node Biopsy in Patients with Early-Stage Breast Cancer: CSBrS Practice Guidelines 2021, in accordance with the Expert Consensus and Technical Operational Guidelines for Sentinel Lymph Node Biopsy guided by blue dye alone in Early Breast Cancer (2018) combined with data from clinical practice in breast surgery in China, providing a reference for breast surgeons in clinical practice in China.

## Level of evidence and recommendation strength

### Level of evidence standard

The level of evidence grading system was developed by referring to the GRADE system combined with findings in clinical studies in China. The levels are classified as Category I, II, III, and IV to quantify the evaluation of the

reliability of the evidence by experts on the compiling committees. To make these guidelines accessible in clinical practice in China, the expert panel preferentially selected Category I and II evidence, as indicated in the guideline evaluation system [Table 1].

### Recommendation strength standard

The recommendation strength of these guidelines combines the GRADE system and the characteristics of clinical practice in China, with four influencing factors, namely the level of evidence, health economics, product equivalence, and accessibility. According to the weight for each characteristic, the recommendations were scored individually by the experts who wrote the guidelines, using a grading system. The recommendation strength was as follows: A (strong recommendation), B (weak recommendation), and C (not recommended) [Tables 2 and 3].

### Recommendation strength review committee

There were 85 voting committee members for these guidelines: 71 from breast surgery departments (83.5%), 4 from medical oncology departments (4.7%), 4 from medical imaging departments (4.7%), 1 from a pathology department (1.2%), 1 from an obstetrics and gynecology department (1.2%), 1 from a radiotherapy department (1.2%), and 3 epidemiologists (3.5%).

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**Table 1: Standard of level of evidence.**

Level of evidence	Standard
I	Based on high-level prospective randomized controlled clinical trials, observational studies or meta-analyses with large sample sizes, internationally-recognized current guidelines and consensus statements, published guidelines and consensus statements from national societies or associations
II	Based on low-level randomized clinical trials, well-designed non-controlled trials or cohort studies, inter-continental professional association guidelines and international conference expert consensus statements, published guidelines and consensus statements from national regional societies or associations
III	Based on case-control studies or retrospective studies, published guidelines and consensus statements from national professional associations, and provincial societies or associations
IV	Based on case reports, scientific hypotheses, regional expert consensus statements and published guidelines and consensus statements from national local societies or associations

**Table 2: Factors influencing the recommendation strength and evaluation standard.**

Influencing factor	Weight/Score	Assignment standard
Level of evidence	60	I: 60; II: 45; III: 30; IV: 15
Health economics	10	Comply: 10; Do not comply: 0
Product equivalence	10	Equivalent products or measures: 10; No equivalent products or measures: 0
Accessibility	20	Good accessibility in Chinese conditions: 20; Poor accessibility in Chinese conditions: 0
Total	100	

**Table 3: Recommendation strength.**

Strength of recommendation	Standard assigned by the experts
A (Strong)	Average total score for the four influencing factors: >80
B (Weak)	Average total score for the four influencing factors: 60–80
C (Not recommended)	Average total score for the four influencing factors: <60

**Target audience**

Clinicians specializing in breast diseases in China.

**Recommendations**

**Recommendation 1: SLNB indications**

SLNB indications	Level of evidence	Recommended strength
1.1 Early-stage invasive breast cancer, axillary lymph node negative in the clinical examination	I <sup>[2-4]</sup>	A
1.2 Ductal carcinoma <i>in situ</i> (DCIS), invasive carcinoma cannot be excluded clinically	I <sup>[5-7]</sup>	A
1.3 cN0 before neoadjuvant therapy and cN0 after neoadjuvant therapy	I <sup>[5,6,8-12]</sup>	A
1.4 cN1 before neoadjuvant therapy and cN0 after neoadjuvant therapy	I <sup>[5,6,8-12]</sup>	A

SLNB: sentinel lymph node biopsy.

**Recommendation 2: SLNB contraindications**

SLNB contraindications	Level of evidence	Recommended strength
2.1 Inflammatory breast cancer	I <sup>[5,6,13]</sup>	A
2.2 Invasive breast cancer with axillary lymph node metastasis confirmed by needle biopsy without neoadjuvant therapy	I <sup>[5,6,14]</sup>	A
2.3 Allergy to the tracer	I <sup>[5,6,14]</sup>	A

SLNB: sentinel lymph node biopsy.

**Recommendation 3: SLNB mapping methods**

Mapping method	Level of evidence	Recommended strength
3.1 Combination of radioisotope and blue dye	I <sup>[15-17]</sup>	B
3.2 Radioisotope	I <sup>[18,19]</sup>	B
3.3 Blue dye	I <sup>[20]</sup>	A
3.4 Fluorescence imaging	I <sup>[21,22]</sup>	A

SLNB: sentinel lymph node biopsy.

Recommendation 4: Clinical problems

4.1 Tracer Selection

Mapping method	Tracer selection	Level of evidence	Recommended strength	
4.1.1	Blue dye	Methylene blue	I <sup>[14,20]</sup>	A
		Carbon nanoparticles	I <sup>[23,24]</sup>	A
4.1.2	Radioisotope	Patent blue	I <sup>[16,20,25]</sup>	B
		Isosulfan blue	I <sup>[15,20]</sup>	B
4.1.3	Fluorescence imaging	Indocyanine green	I <sup>[16,26-28]</sup>	B
			I <sup>[22,27,29]</sup>	A

4.2 Injection site

Injection site	Level of evidence	Recommended strength
Intradermal or subcutaneous around the affected areola <sup>*,†</sup>	I <sup>[30,31]</sup>	A

\*Tumor parenchyma and tumor periphery can also be considered as tracer injection sites. †The injection site should be in accordance with the appropriate tracer instructions.

4.3 SLNB and neoadjuvant therapy

Axillary lymph node status	SLNB selection	Level of evidence	Recommendation strength	
4.3.1	Initial cN0 patient	SLNB before NAT <sup>*,†</sup>	I <sup>[3,5,6,10,32-35]</sup>	A
		SLNB after NAT	I <sup>[3,5,6,10,32-35]</sup>	A
4.3.2	Patients with initial cN1 and converted to cN0 after NAT	SLNB after NAT	I <sup>[5,6,10-12,32,36,37]</sup>	A
4.3.3	Patients with initial >cN1 and converted to cN0 after NAT	Direct ALND	I <sup>[5,6,10-12,32,36,37]</sup>	A
		No SLNB, ALND directly	I <sup>[5,6,32]</sup>	A
4.3.4	Patients with initial cN+ and remaining cN+ after NAT	No SLNB, ALND directly	I <sup>[5,6,32]</sup>	A

NAT: neoadjuvant therapy; SLNB: sentinel lymph node biopsy; ALND: axillary lymph node biopsy; cN0, clinical node negative; cN+, clinical node positive; cN1, clinical node stage 1. \*Accurate information for axillary lymph node staging can be obtained by SLNB before neoadjuvant therapy for patients with cN0. †When N stage affects patients' comprehensive treatment decision, SLNB should be performed before neoadjuvant therapy.

Recommendation 5: Pathological diagnosis

Diagnostic method

Diagnosis timing	Evaluation method	Level of evidence	Recommended strength
Intraoperative evaluation	Rapid frozen section pathological examination	I <sup>[32,38-42]</sup>	A
Post-operative evaluation	Paraffin section and immunohistochemical examination	I <sup>[32,43-45]</sup>	A

Recommendation 6: Follow-up surgery for different SLN status

6.1 SLNB for early-stage breast cancer with initial surgery

SLN status	Axillary surgery	Level of evidence	Recommended strength	
6.1.1	SLN-negative	No subsequent ALND	I <sup>[3,5,6,34,35]</sup>	A
6.1.2	1–2 positive SLNs <sup>*</sup>	T1–2, breast-conserving surgery, whole-breast radiotherapy planned, ALND can be exempted	I <sup>[5,6,46,47]</sup>	A
		Total mastectomy, axillary radiotherapy planned, ALND can be exempted	II <sup>[48,49]</sup>	B
6.1.3	≥3 Positive SLNs	ALND	I <sup>[5,50,51]</sup>	A

6.2 SLNB after neoadjuvant therapy

SLN status	Axillary surgery	Level of evidence	Recommended strength	
6.2.1	SLN-negative <sup>†</sup>	No subsequent ALND	I <sup>[5,10,11,26,52]</sup>	A
6.2.2	SLN-positive <sup>‡</sup>	ALND	I <sup>[5,10,11,26,52]</sup>	A

SLNB: sentinel lymph node biopsy; ALND: axillary lymph node biopsy. \*When SLN status is positive, and there is no radiotherapy planned or radiotherapy is not elected, ALND should be performed regardless of breast-conserving or mastectomy. Direct ALND can be a reasonable selection when SLN is positive. †There is a lack of standard double tracer techniques in SLNB in clinical practice in China. Therefore, ALND can still be used in patients with initial cN1 status converted to cN0 after neoadjuvant therapy. ‡Patients with any degree of residual tumor cells detected in SLNs after neoadjuvant therapy should be considered SLN-positive.

## Discussion

The SLN concept originated from clinical studies in penile cancer, and the term is defined as one or a group of lymph nodes that first receive regional lymphatic drainage from the tumor and then develop tumor metastasis. In the early 1990s, Krag *et al*<sup>[28]</sup> successfully used radionuclide tracing, and Giuliano *et al*<sup>[53]</sup> used isosulfan blue dye in SLNB of breast cancer. The Milan 185 study,<sup>[4]</sup> ALMANAC study,<sup>[3]</sup> and NSABP B32 study<sup>[34]</sup> laid the foundations for SLNB in the staging surgery of axillary lymph nodes in breast cancer; therefore, approximately 70% of breast cancer patients are exempt from ALND. The CBCSG-001 study in China reported similar conclusions.<sup>[54]</sup> SLNB has the advantages of fewer complications and less trauma than ALND,<sup>[1]</sup> and has become the preferred surgical procedure for staging axillary lymph nodes in breast cancer.<sup>[5]</sup>

The clinical evaluations for axillary lymph node staging in early invasive breast cancer recommended by the National Comprehensive Cancer Network (NCCN) and Chinese Society of Clinical Oncology (CSCO) guidelines are clinical physical examination and ultrasonographic examination. If the lymph nodes are not palpable during physical examination, staging can be considered as cN0. Ultrasonographic examination can evaluate the shape of the axillary lymph nodes, measure the size of the lymph nodes and the cortical thickness, and confirm blood flow. The ultrasonographic features of negative lymph nodes are a regular shape, presence of a normal hilar structure, uniform cortical thickness and echo uniformity, maximum cortical thickness <3 mm, and portal blood flow.<sup>[55]</sup> The expert panel recommends ultrasonography as the preferred imaging technique for axillary lymph node assessment in breast cancer.

SLNB is preferred for early invasive cN0 breast cancer. In patients with ductal carcinoma in situ diagnosed by core needle biopsies, the potential to misinterpret the tumor type and miss invasive carcinoma should be considered. Therefore, SLNB should be performed when invasive carcinoma cannot be excluded.

The combined use of radioisotopes and blue dye has been widely recognized,<sup>[56]</sup> and the expert panel recommends that qualified hospitals should perform dual-tracer SLNB. However, it should be noted that the surgeon must be qualified to use radioisotopes. Because patent blue violet and isosulfan blue are not approved in China, and the clinical application of radioisotopes is strictly managed, this mapping method cannot be widely used in China. Therefore, methylene blue, carbon nanoparticles, and indocyanine green are often selected as SLNB tracers. The SLNB detection rate and false negative rate of methylene blue<sup>[57]</sup> and carbon nanoparticles<sup>[58]</sup> have been clinically confirmed. The expert panel recommends methylene blue<sup>[59]</sup> and carbon nanoparticles for SLNB in early breast cancer (see the appendix for the technical specifications). Combining indocyanine green and methylene blue is also a reasonable tracing technique for SLNB.<sup>[21,27]</sup> The expert panel recommends that the combination of fluorescence imaging and blue dye can be used to improve the detection rate,<sup>[60,61]</sup> if conditions permit.

The 8<sup>th</sup> edition of the American Joint Committee on Cancer (AJCC) breast cancer staging system<sup>[62]</sup> contains specific provisions regarding the SLN detection number and status determination. The number of SLNs detected in breast cancer must be less than six; otherwise, the footnote “Sn” cannot be used for annotation. The definition of SLN status is listed in the appendix.

The reported clinical false-negative rates for SLNB are generally < 10%.<sup>[3,4,34]</sup> Surgeons should be trained to reduce the SLNB clinical false-negative rate associated with surgical procedures.<sup>[63]</sup> In clinical practice in China, intraoperative frozen section pathological examination is the main pathological evaluation in SLNB intra-operatively, with a reported false-negative rate of approximately 10%.<sup>[64]</sup> Currently, the expert panel believes that the frozen section pathological assessment of SLNs is appropriate in China, and suggests that we should strictly implement specimen sampling and standardize pathological reporting processes according to the standards of the College of American Pathologists<sup>[43]</sup> to reduce the pathological false-negative rate of SLNB. Using intraoperative immunohistochemical staining to determine SLN status is not recommended.

Studies have shown that patients with T1–2 breast cancer undergoing breast-conserving surgery, with 1–2 positive SLNs, can be exempted from ALND under the condition of postoperative adjuvant whole-breast radiotherapy, without influencing disease-free survival (DFS) and overall survival (OS).<sup>[47,65]</sup> The expert panel agrees to exempt such patients from ALND. There is no research evidence regarding whether patients with 1–2 positive SLNs undergoing total mastectomy can be exempted from ALND if they undergo adjuvant radiotherapy, and the expert panel believes that ALND exemption should be determined carefully. Patients with positive SLNs unable to receive postoperative radiotherapy should undergo ALND regardless of the surgical breast procedures. According to the expert panel, in accordance with the characteristics of SLNB in clinical practice in China, patients with any degree of residual tumor cells detected in SLNs after neoadjuvant therapy should be considered SLN-positive,<sup>[66]</sup> and ALND is recommended.

Studies have confirmed that SLNB after neoadjuvant therapy is safe for initial cN0 patients.<sup>[67]</sup> The expert panel agrees that patients with initial cN0 can choose to undergo SLNB before or after neoadjuvant therapy according to their specific conditions. When SLN status is of great significance to the overall treatment decision, SLNB is preferred before neoadjuvant treatment.<sup>[5]</sup>

Studies have confirmed the clinical safety of SLNB, and the detection rate and false negative rate after neoadjuvant therapy.<sup>[10-12]</sup> After neoadjuvant therapy in initial cN1 patients, SLNB can be exempted from ALND when performing SLNB after neoadjuvant therapy with dual-tracer techniques and with two or more negative SLNs.<sup>[68,69]</sup> Because most medical institutions in China are unable to choose the combined isosulfan blue and radioisotope tracer technique for SLNB, the expert panel believes that Chinese clinicians should be cautious when exempting patients from ALND in this situation.



With the emergence of evidence-based medicine, the related concepts of SLNB are constantly being updated, and these changes affect clinical practice. These changes ensure patient safety during tumor treatment, minimize surgical complications, and improve patients' quality of life.

## Appendix

### Appendix 1. Surgical recommendations for SLNB with methylene blue dye for early breast cancer

The arrangement of endothelial cells in human capillaries is relatively tight, with an intercellular space of only 30 to 50 nm. However, the intercellular space in the lymphatic capillaries is larger, at approximately 100 to 500 nm. Therefore, if the diameter of the SLNB dye tracer particles is too small, the tracer will enter the capillary and blood circulation simultaneously as well as spread easily in the lymphatic vessels and lymph nodes, resulting in staining of the inferior lymph nodes, and affecting the accuracy of SLNB. Dyes with a particle diameter of 50 to 200 nm have the advantage of specific aggregation in the lymphatic system, and do not enter capillaries easily. Additionally, dyes with a larger diameter can remain in SLNs longer, which is helpful regarding the time requirement during surgery.

Methylene blue is an aromatic heterocyclic compound. Its chemical name is 3,7-bis (dimethylamino) phenazathionium chloride, and the dye has a molecular weight of 319.858 Da. Methylene blue is commonly used as a chemical indicator, dye, and biological dye in medicine, and is excreted in the urine without being metabolized after intravenous injection.

According to the Pharmacopoeia of the People's Republic of China, methylene blue is injected intradermally and intravenously, and not subcutaneously, intramuscularly, or intrathecally. The subcutaneous and intramuscular routes cause necrosis, and the intrathecal route causes paralysis.<sup>[70]</sup> Methylene blue has been reported to cause allergic reactions<sup>[71]</sup> and fetal malformation, and the use of methylene blue in pregnant patients with breast cancer is controversial.<sup>[72]</sup> Methylene blue has also been associated with serotonin syndrome.<sup>[73]</sup> The time required for methylene blue to pass through lymphatic vessels is 5–15 min. Because of its low molecular weight, it is not the best lymphatic tracer; however, with its low price and because it is easy to obtain, many hospitals in China still use methylene blue as an SLNB tracer.

## 1. Preoperative preparation

### 1.1 Confirm that the patient has no surgical contraindications and prepare the axillary skin.

### 1.2 Obtain signed informed consent.

## 2. Positioning

The supine position is recommended. The affected upper limb is abducted 90° and rotated outward, and the axilla is

fully exposed by placing the arm on a supporting board or flat table.

## 3. Procedure

### 3.1 Disinfection

Routine disinfection.

### 3.2 Anesthesia

General anesthesia is used for SLNB if performed simultaneously with breast surgery; local anesthesia or general anesthesia can be used for SLNB alone.

### 3.3 Dye injection

The areolar area is rich in lymphatic vessels. Selecting 1–3 injection sites in the outer upper area of the areola is recommended. Use a 1-ml syringe, with a total injection volume of 0.1 to 0.5 ml by intradermal injection. During the injection, proper pressure should be applied to form a bleb, and the dendritic intradermal reticular lymphatic network should be visualized. Surgery can begin after applying appropriate pressure.

### 3.4 Axillary incision selection

The incision location is crucial for the accurate identification of blue-dyed SLNs. The recommended anterior border is the lateral border of the pectoralis major, and the recommended posterior border is the anterior border of the latissimus dorsi. An incision measuring approximately 4 to 5 cm is made along the dermatoglyph at the lower edge of the axillary hair area. If the incision position is too high, it may exceed the SLN level, and the blue-dyed lymphatic vessels will not be visualized. If the incision position is too low, it is necessary to dissect a longer path along the blue-dyed lymphatic vessels to find the SLNs. During total mastectomy, SLNB can also be completed by dissecting along the subcutaneous blue-dyed lymphatic vessels to the axilla after the upper breast flap is dissected free.

### 3.5 Key points in the operation

The superficial lymphatic vessels are located in the deep dermis, gradually flow in the axillary direction, enter the deep layer of the superficial fascia, finally penetrate the deep layer of the coracoclavicular fascia, and flow into the axillary lymph nodes. Therefore, the blue-dyed lymphatic vessels can be observed directly in patients with a lower incision after incising the skin and subcutaneous fat. In patients with a higher incision, the blue-dyed lymphatic vessels can only be visualized after deep incision of the superficial fascia, and even can only find blue-dye lymph nodes. The blue-dyed SLNs can be found by dissecting along the blue-dyed lymphatic vessels to the axilla. The blue-dyed lymphatic vessels are transected, and the SLNs are completely excised with a small amount of adjacent adipose tissue. Attention should be paid to whether there are residual blue-dyed lymphatic vessels behind the excised SLNs to avoid missing an SLN. The excised SLNs are then sent for frozen pathological evaluation. In breast-conserving surgery, ligat-

ing the transected proximal ends of the blue-dyed lymphatic vessels can reduce lymph leakage. When identifying blue-dyed lymphatic vessels and SLNs, the lymphatic vessels should not be transected to avoid contaminating the operative field and increasing the operative difficulty.

### 3.6 SLN confirmation

The first or several blue-dyed lymph nodes reached by the blue-dyed lymphatic vessels are SLNs. For multiple blue-dyed lymphatic vessels, attention should be paid to the first blue-dyed lymph nodes.

### 3.7 Surgical drainage

There is no need for indwelling drainage after closing the surgical field. If breast-conserving surgery and ALND are needed, a negative-pressure drain should be placed.

## 4. Complications and prevention

### 4.1 Bleeding

Generally, the SLNB incision is small, and the operative visual field is poor in patients with fat in the axilla or accessory mammary tissue. Inexperienced surgeons or those unfamiliar with the local anatomy may injure blood vessels and even axillary arteries and veins. When the operation is difficult, the incision should be enlarged to fully expose the operative area and attention paid to fine dissection layer by layer, with strict hemostasis.

### 4.2 Wound hematoma

Lymphatic vessels and lymph nodes are part of the vascular system. Improper treatment of the large afferent lymph vessels may lead to postoperative hemorrhage and hematoma formation. Surgeons should pay attention to the management of vessels supplying the SLNs.

### 4.3 Seroma

Ligating the proximal lymphatic SLN vessels is recommended during SLNB, when this procedure is performed as the sole procedure. Additionally, closing the coracoclavicular fascia and superficial fascia can also avoid seroma formation in the deep incision.

SLNB as the preferred technique in axillary lymph node surgical staging of breast cancer has reached consensus. Blue dye tracers for SLNB are simple and reliable to use, and the operative process is intuitive and easy to master, which is suitable for promotion throughout China, especially in primary hospitals.

## Appendix 2. Specifications for pathological examination of SLNB in breast cancer

### 1. SLN pathological diagnosis in breast cancer

#### 1.1 Intraoperative SLN pathological diagnosis

Intraoperative frozen tissue sections or cytological impression smears are recommended for SLN pathological

examination.<sup>[6]</sup> Cytology of impression smears is easy to perform, with high specificity but low sensitivity.<sup>[74]</sup> In contrast, frozen tissue section evaluation can accurately measure the size of the metastatic foci and determine whether there is extranodal invasion. However, intraoperative SLN pathological examination also has limitations. The reported false-negative rate for intraoperative frozen tissue section SLN pathological diagnosis ranges from 10% to 20%.<sup>[64,75]</sup> Standardized sampling is very important to control the false-negative rate, and the remaining tissue from frozen sections should be examined by paraffin embedding and sectioning.

#### 1.2 Postoperative SLN pathological diagnosis

Routine paraffin-embedded hematoxylin and eosin (H&E) section histological examination is the gold standard for SLN diagnosis, and cannot be replaced by molecular diagnosis. In particular, care should be taken to ensure adequate specimen size. All macrometastases must be confirmed by histological examination. Immunohistochemical techniques are not recommended routinely for screening for micrometastasis and isolated tumor clusters (ITCs) in SLNs.

## 2. Intraoperative SLN pathological gross examination and sampling<sup>[43]</sup>

### 2.1 Gross examination and sampling for positive SLNs

The sizes of the lymph node and the metastatic foci should be measured in the metastatic lymph node specimens identified by the naked eye. In parallel sections along the largest plane, at least one piece of tissue containing the largest metastatic focus is sampled, including the extranodal infiltrating part outside as much as possible.

### 2.2 Gross examination and sampling of negative SLNs

Identifying SLN macrometastases is critical to determine the prognosis, and all macrometastases should be detected, ideally. Each lymph node is sectioned in parallel along the largest plane, with a thickness of not >2 mm (to avoid missed macrometastases), with all lymph nodes examined histologically. At least one satisfactory H&E-stained section is prepared for each slice. Multi-level sections are not recommended when the standard tissue section thickness is <2 mm.

## 3. SLN assessment criteria

### 3.1 Number of detected SLNs

Histopathological examination should be performed on all SLN lymph nodes submitted for clinical examination. The recommended number of SLNs is less than six in the 8<sup>th</sup> edition of the American Joint Committee on Cancer (AJCC) breast cancer staging system<sup>[62]</sup>; otherwise, the SLN footnote “Sn” should not be used.

### 3.2 SLN status evaluation

Macrometastasis and micrometastasis are defined as SLN-positive; isolated tumor cell clusters and no metastasis are defined as SLN-negative.

### 3.2.1 SLN-positive status

Macrometastases: maximum diameter of the tumor deposit >2.0 mm, stage  $\geq$ pN1.

Micrometastases: maximum diameter of the tumor deposit >0.2 mm but  $\leq$ 2.0 mm or >200 tumor cells in one lymph node section. Regardless of how many lymph nodes are involved, if all contain micrometastases, the stage is pN1mi.

### 3.2.2 SLN-negative

Isolated tumor cell clusters: When tumor cells are scattered in small clusters with a single or maximum diameter  $\leq$  0.2 mm or  $\leq$ 200 tumor cells are identified in one lymph node section, and there is no evidence of malignant activity (such as no proliferative or interstitial reaction), the stage is pN0 (i+).

No metastasis: No tumor cells are found in the section.

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### Conflicts of interest

The expert committee for these guidelines declares no conflict of interest. These guidelines are a reference for breast disease specialists in clinical practice. However, the guidelines are not to be used as the basis for medical evaluation, and do not play an arbitrating role in the handling of any medical disputes. The guidelines are not a reference for patients or non-breast specialists. The Chinese Society of Breast Surgery assumes no responsibility for results involving the inappropriate application of these guidelines, and reserves the right to interpret and revise the guidelines.

**Data sharing:** no additional data available.

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