 doi:10.20944/preprints202204.0132.v1

Article

Sentinel Lymph Node in Breast Cancer: An Innovative Techniques

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Abstract: (1) Background: Sentinel lymph node biopsy assumes importance in the search for metastases, especially in patients with malignant breast disease. Our study approaches the new techniques to prevent complications such as possible postoperative seroma formation, pain or hypoesthesia of the axillary cord and medial arm surface, as well as motor deficits in a preventive manner to avoid disabling outcomes and presents initial data from its experience with the sentinel lymph node biopsy technique. (2) Methods: There are mainly two radioactive tracer detection techniques and a new technique using a radiotracer called Sentimag-magtrace. The positive lymph node is located and removed to perform histologic analysis. In our study, we evaluate 100 patients who underwent breast cancer surgery (3) Results: our experience allowed us to calculate the identification rate with the different methods of sentinel lymph nodes by radioactive tracer 88.9 % vs magnetic tracer technology (Sendimag) 89.5%. (4) Conclusions Thus, this technique avoids radiation exposure for both patients and health care providers, as well as reducing costs and time.

Keywords: SLNB; SPIO; ALND; LS; superparamagnetic iron oxide nanoparticles

1. Introduction

The biopsy of the sentinel lymph node (SLN) assumes a high importance for metastases research, especially in patients with malignant breast disease, where the metastatic spreading generally occurs through the lymphatic system in a progressive manner, or rather without jumps of lymph nodes; this technique, with high reliability, allows to avoid the patient an axillary lymph node dissection (ALND) and all of its complications [1, 2].

The various lymphocytes can be found in aggregates, which are the name of lymphoid tissue. When these aggregates are found in the mucous membranes connective tissue, which is generally abundant in the cavities of the body that communicate with the outside, such as the respiratory, digestive, urinary or reproductive tract, take the name of lymphoid tissue associated with mucous membranes (also known as MALT Mucosa Associated Lymphatic Tissue). In some areas of the body, lymphocytes and macrophages can join to form aggregates called lymphatic or follicle nodules, at which the lymphocytes always recirculate ready to activate an immune response. These nodules are characteristic of lymph nodes, tonsils and appendix.

The most interesting lymphoid organs on SNL technique are obviously the lymphnodes; these are the largest lymphoid organs, they are scattered throughout the body, and carry out the filtration functions of the lymph and activation site of lymphocytes B and T. The lymph node looks like a bean-shaped oval organ that usually does not It exceeds the three centimeters in length and on one of its sides converges to form a recess. The lymph nodes are covered by a connective fibrous capsule from which the sectors called trabeculae depart which deepen to divide the organ into compartments. Between the capsule and the parenchyma there is a small space called subcapsular breast which contains reticular fibers, or collagen fibers, macrophages and dendritic cells. The parenchyma is divisible in a cortical part-shaped part, which covers almost all the circumference of the lymph node, and in a more internal medullary part than one.

The first is mainly composed of lymphatic nodules separated from that in a state of activation against a pathogen take a germinative center where the B lymphocytes multiply and differ in plasma cells; the second one is composed of a sort of network of mid-collar cords composed of lymphocytes, plasma cells, macrophages, reticular cells and reticular fibers. Furthermore, both the cortical and the medullary have respective breasts in continuity with the subcapsular breast.

The lymph enters the lymph nodes on their convex surface, through the different ventilated manifold vessels, flows in the subcapsular breast and then slowly through the breasts of the cortical and medullar where, by entering into contact with the cells of the immunity present, is filtered by the various substances extraneous; later it comes out through the only effective lymphatic vessel, which together with blood vessels, emerges from the hilium.

The lymph nodes, due to their role of stations along the course of a vessel, as well as from pathogenic agents, can be reached by metastasis; by metastatic diffusion of tumors means that phenomenon in which neoplastic cells detach from primitive tumor, spread to other blood and / or lymphatic organs. They continue to proliferate uncontrollably, determining the formation of secondary neoplasms. Due to the high permeability of lymphatic capillaries, neoplastic cells easily penetrate them inside and spread in the sap. They then localize in the regional lymph nodes where they proliferate, replacing the lymphoid cells present; once the neoplasia is well implanted in a lymph node, the cells can further spread to other lymph nodes.

However, if the metastasis is detected early enough, the malignant pathology can in some cases be eradicated by removing not only the primary tumor, but also the nearest loco-regional lymph nodes. The example is represented by malignant breast pathology, which was often treated with the removal of the neoplastic mass through a partial or total mastectomy, combined with the removal of the axillary lymph nodes also called axillary lymphadenectomy (ALND). However, this technique has many complications; the main one is represented by the lymphedema of the upper limb (abnormal accumulation of lymph, temporary or permanent), caused by the interruption of lymphatic vessels that drain the flow of lymph from the limb itself, with an incidence of about 10%.

Other complications include the possible formation of a post-operative seroma, pain or hypoesthesia of the axillary cavity and medial surface of the arm, as well as motor deficits; the latter may be due either to accidental nerve injury during surgery, or more frequently to the formation of fibrous scar tissue that limits limb movement. It is precisely in order to prevent the invalidating outcomes of ALND that the technique of sentinel lymph node biopsy becomes relevant.

Sentinel lymph node is the first lymph node that receives lymph from a tumor and is therefore likely to be the first to be reached by metastases. Through biopsy and histological analysis of this lymph node, it is possible to determine its involvement or not by metastases and consequently refer the patient to axillary lymph node emptying. Metastases detected by histological examination can be classified into macrometastases, if they have a diameter greater than or equal to 2 mm, micrometastases if the extension is between 0.2 and 2 mm, and isolated tumor cells (ITC) in case of a total diameter of less than 0.2 mm. Aim of our study is to approach the new techniques to prevent complications such as the possible formation of a post-operative seroma, pain or hypoesthesia of the axillary cord and medial surface of the arm, as well as motor deficits

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precisely to avoid disabling outcomes and presents the first data of its experience with the sentinel lymph node biopsy technique [2,3].

2. Materials and Methods

The study was approved by the Sapienza University Research Federated Athensis n. C26F09B5E5. We considered in our study 100 patients who underwent with breast cancer diagnosed with Mammography and histological examination. Inclusion criteria were: (1) any patient who needed to localize an intractable breast lesion; (2) any patient who needed a sentinel lymph node biopsy; (3) the patients were collected from January 2019 and Jan 2021. Comparisons were made between patients with different localization methods: with radiative tracer and with magnetic tracer technology (SendiMag). Baseline demographic data were collected at the time of surgery and outcomes were recorded. Staging, lymph node status, lymph node detection rates, and complications were collected.

2.1 Vital dye technique

Vital dyes are substances that are injected into the lymph nodes and allow their localization by presenting a bluish coloration. There are various types such as isosulfan blue (Isosulfan Blue), methylene blue (Methylene Blue) and sulphan blue, although the most widely used is Patent Blue V (Patent Blue-V) which consists of an internal salt or calcium compound of diethylammonium hydroxide.

The technique is that the dye can be injected subdermally or peritumorally. In the first case, after the induction of general anesthesia, 0.2- 0.4 ml of Patent Blue-V is injected on the skin projection of the neoplasm, and a gentle massage of the injected area is performed to facilitate the progression of the dye towards the axillary cavity. In the second case it is necessary to inject larger volumes (2 to 4 ml) in two or more peri-tumoral points and also in this case it is necessary to massage the injection area to obtain a more rapid diffusion of the dye towards the axillary cavity. However, the subdermal route is preferred because the smaller volume injected reduces the skin tattoo that is created by diffusion from the injected area, making it easier to find the sentinel lymph node; moreover, the rich lymphatic vascularization of the dermis allows the dye to reach the sentinel lymph node more quickly.

The removal of the lymph node can begin after about 15 minutes from the injection, going to find the bluish area where the dye has risen.

This method is less used but still very effective in detecting the sentinel lymph node, important contraindications are the blue marks that it leaves for a long time on the patient's skin and also hypersensitivity reactions of anaphylactic type with a probability of about 2% [3,4,5].

2.2 Radioactive tracer technique

In this technique the radiopharmaceutical 99mTecnezio Nanocoll is used, i.e., colloidal particles of human albumin, with a size between 20 and 80 nm (nanocolloids), labeled with the metastable radioisotope Technetium 99 (99mTc). Sentinel lymph node identification can be performed in two moments: before the operation by means of a breast lymphoscintigraphy and during the operation by means of a radio-guided surgery probe; lymphoscintigraphy can be performed in turn the day before the operation or the same day at least 1-2 hours before the operation.

The radioactive tracer (99mTc) is injected, by the nuclear physician, generally with a dose of 0.2 milliCuries (mCi) (in heavy weight patients the dose is increased to 0.4 mCi), in a solution ranging from 0.2 to 0.4 ml in volume, using a 25 Gauge needle. An excessive volume of the injected radiopharmaceutical collapses the lymphatic capillaries and hinders accumulation on the sentinel lymph node.

In case of palpable nodules, the localization is simple, while in case of non-palpable lesions, the injection is based on neoplastic opacities detectable by ultrasound guidance or on an aggregate of tumor microcalcifications detectable under mammographic stereotactic guidance.

Basically, the injection can be performed in three modalities:

- Subdermal injection: this injection occurs in the subcutis at the lesion and allows a faster migration of the radiopharmaceutical, taking advantage of the rich lymphatic vasculature of the dermis.

- Perilesional injection: intraparenchymal injection around the mass, usually performed in deep neoplasms.

- Periareolar injection

Intratumoral inoculation is not recommended because inflammation is often created around the lesion and the 99mTc nanocolloid tracer is unable to pass through this layer of inflamed tissue.

After the injection, a gentle massage is given to the site to facilitate lymphatic drainage and wait for the radiocolloid to reach the lymph node.

At this point, lymphoscintigraphy can be performed using a gammacamera, a device found in nuclear medicine departments, which converts the gamma photons emitted by the decays of the radionuclide inside the patient into images that can be viewed on a monitor.

Immediately after the administration of the radiopharmaceutical it may be useful, but not mandatory, a dynamic acquisition of 10-15 frames lasting 1 minute, to document the initial kinetics of tracer distribution; after about 15 minutes static planar acquisitions are made in two or three projections but in case of poor migration of the radiocolloid are also acquired after 3 and 18 hours.

The first and most revealing projection is the 45° anterior oblique (right or left depending on the breast affected by the lesion, or both if both are involved); it is performed keeping the surface of the gammacamera head as parallel as possible to the axillary cavity and allows to better distinguish the inoculation point from the sentinel lymph node, which will appear as the first one draining the neoplastic tissue. The second is the anterior projection, important for the lymph nodes of the internal mammary chain. Finally, lateral projection images can be acquired.

After the acquisitions, with the help of a Cobalt57 point source (57Co) the skin projection of the same lymph node is highlighted and marked with an indelible ink.

The lymphoscintigraphic image available before surgery is of great value as it allows to detect the location and the presence of one or more lymph nodes and allows to direct the surgeon before surgery, allowing a more appropriate planning of the same.

The radiopharmaceutical used for sentinel lymph node biopsy (SLNB) is 99mTc Nanocoll, i.e., nanocolloidal particles of human albumin labeled with metastable Technetium 99; Nanocoll is prepared using human serum albumin obtained from human blood donors, tested in accordance with European Community regulations and found to be non-reactive for hepatitis B surface antigens (HBsAg), human immunodeficiency virus antibodies (anti-HIV 1/2), hepatitis C virus antibodies (anti-HCV). These particles, having a maximum diameter of 80 nm, easily enter the lymphatic capillaries, thus being drained and captured by the lymph nodes. In rare cases, hypersensitivity reactions may occur.

99mTc is a metastable isotope of Technetium (metallic element with Z=43) produced by decay of 99Molybdenum (99Mo). From a physical point of view 99mTc has optimal characteristics as it is a pure gamma emitter with photon energy at 140 KeV (ideal for imaging with gamma camera/SPECT), has a half-life of 6 hours (long enough to be transported from a production site to a site of use and short enough to reduce the dose to the patient and his companions) and is easily available. Chemically, 99mTc is eluted from the generator column as technetium pertechnetate (99mTcO4-).

The production of 99mTc is in fact based on the use of 99Mo/99mTc generators. The generator is a system by which a parent radionuclide with a relatively long half-life

 doi:10.20944/preprints202204.0132.v1

(about 67 hours for 99Mo), you get a radionuclide child with a short half-life (6 hours for 99mTc) and consists of a cylindrical lead container that contains a column of ion exchange resin, is the different adsorption on the column of radionuclide parent and child that allows you to remove from the generator, after appropriate elution, the radionuclide child. The elution of the column is done with a solvent, in this case a physiological solution, which allows to separate the radionuclide son from the column without altering the bond of the radionuclide father with the column itself, thus obtaining an eluate with a high radiochemical purity. The column is connected to the outside by two small tubes which, starting from the two ends of the column, end up in as many needles fixed in two cavities at the top of the generator. To elute the 99mTc it is sufficient to insert, in one of the two needles, a glass vial with a pierceable rubber cap, containing sterile physiological solution; then insert in the second needle another vial, inserted in a shielded container (lead or tungsten), in which an air vacuum has been created. The depression created by the vacuum causes the emptying of the vial containing the physiological solution that, interacting with the resin column, removes the 99mTc that, at the end of the elution, will be all contained in the second vial. Immediately after elution, the resin column contains only 99Mo, but since the decay 99Mo → 99mTc continues, new 99mTc starts to form immediately.

2.3 Magnetic tracer technology

In recent years another method has been developed, which does not involve the use of radioactive material for the identification of the sentinel lymph node (LS), with which almost all identifications are performed today, but the use of a non-radioactive magnetic tracer; this represents a real revolution in the approach to the procedure. This system consists of the Sentimag probe and the Magseed magnetic marker. the marker is placed under ultrasound guidance up to 30 days before surgery. During surgery, we use Sentimag to precisely localize the Magseed and thus the lesion. This new tracer, which is commercially available only under the name of Sienna + ®, consists of a black-brown aqueous suspension composed of nanoparticles of superparamagnetic iron oxide (SPIO superparamagnetic iron oxide) coated with carboxydextran that must be used only in conjunction with a Sentimag® magnetometer [6,7]; the coating of carboxydextran while maintaining biocompatibility, prevents the agglomeration of these particles that having a diameter of about 60 nanometers, are small enough to be drained into the lymphatic capillaries.

The procedure is similar to that with the radioactive tracer but only in the operative phase. A volume of about 5 ml, consisting of 2 ml of magnetic tracer and 3 ml of saline solution, is injected in the periareolar or perilesional area and for 5 minutes the inoculation area is massaged in order to speed up the lymphatic drainage. After about 20 minutes (in case of elderly or overweight patients the migration of particles requires more time) the search for the sentinel lymph node is started by passing the magnetometer probe along the axillary cord. Once a discrete signal is detected, the incision is made and the search for signal from the inside; also, in this method access can be made by exploiting a previous surgical breach.

The SentiMag instrument exploiting the principle of magnetic susceptibility, generates an alternating magnetic field that magnetizes transiently the iron oxide particles of Sienna; these respond with an induced magnetic field of low intensity, with the same direction and direction of the external field applied, (Superparamagnetism) which is then detected by the probe itself.

The presence of nanoparticles will then be detected by producing a sound and a signal on the display of the device, whose intensity will be proportional to the intensity of the induced magnetic field that will be the greater the proximity to the iron particles, collected mainly in the sentinel lymph node. The surgeon then, in addition to locating the LS in the point of greatest signal, will be able to do so visually thanks to the brown coloration that the magnetic tracer gives to the lymph node; it can then be removed and

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histological examination performed. This process is repeated until any remaining lymph node has a signal reading of less than 10% of the first LS removed.

The magnetic tracer cannot be used in patients with hemosiderosis (iron overload disease) or with previous hypersensitivity reactions to dextran compounds [8].

The multicenter study SentiMag was the first to evaluate the magnetic technique for sentinel lymph node biopsy (SLNB sentinel lymph node biopsy) comparing it with the standard procedure (radiopharmaceutical with or without vital dye); it was demonstrated that the new method has a capacity of LS identification substantially equivalent to the method with radioactive tracer (94.5% Sienna+ vs 95% 99mTc). In the MagSNOLL study it is shown how, after intratumoral injection, the magnetic tracer allows the localization of non-palpable breast lesions. Another important property of Sienna+ is that of possessing characteristics similar to the superparamagnetic contrast agent used in MRI; this means that once injected, lymph nodes could be visualized through an MRI of the axillary cavity, in which an inhomogeneous uptake of Sienna in the sentinel lymph node can help identify a metastatic formation, thus replacing preoperative breast lymphoscintigraphy [9,10].

3. Results

We considered in our study 100 (median age 62±6 age, from 55 years old to 70 years old) patients who underwent surgery for a T1a, b, and c -T2 stage less than 2.5 cm breast cancer diagnosed Table 1 show the anamnestic notice of the population. The readings obtained from the two methods show that the data obtained are comparable (Table 2). We performed for sentinel lymph node diagnostics 60 traditional scintigraphy and 40 identifications with the Sendimag (Table 2). We report the complication for as the main one is represented by the lymphedema with an incidence of about 10% (Table3).

Table **1. Anamnestic data of the population**

Age at cancer diagnosis (years; mean)	**45.3±10**
Menopausal status (%)	
Menopause	44.8
No menopause	55.2%
Age at menarche (years, mean)	13.6±3.8
Lactation for at least 3 months (yes, %)	43.%
Mammographic breast density (%)	
BI-RADS 1-2 (no dense breast)	48.9%
BI-RADS 3-4 a, b, and c (dense breast)	51.1%
Suspicious microcalcifications	16.4%
Discordance (>10 mm) between mammographic and US detection of the main in-	12%

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dex lesion and/or its dimensions (%)	
Positive for BRCA1/2 (%)	2.4%
First-degree family history of breast carcinoma* (%)	23.2%
Discordance (>10 mm) between mammo-graphic and MR detection of the main index lesion and/or its dimensions (%)	0.7%

Table 2. Methodic Identification rate.

Technique	Identification Rate %	Number of patients
Radiative tracer	88.9	60
Magnetic tracer technology (Sendimag)	89.5	40

Table 3. Complications

Technique	Title 2	Title 3
Radiative tracer	upper limb lymphedema	15%
Magnetic tracer technology (Sendimag)	upper limb lymphedema	4% [1]

4. Discussion

The sentinel lymph node (LS) technique is performed in those patients with biopsy-proven malignant breast disease that meet certain criteria, without which the examination would not be useful. Most of them are referable to the TNM classification, which is an international system of classification of malignant tumors, from which the stage of the disease can be derived [11,12].

This classification consists of three main parameters as indicated by the name:

- T parameter indicates the size of the primary lesion and can take values from 1 to 4. It can also be is or in situ which indicates an intraepithelial carcinoma that has the morphological characteristics of malignancy but without the infiltrating capacity.

- The parameter N indicates the status of lymph nodes close to the tumor, and is 0 when they are completely unharmed, otherwise it can be 1, 2, 3 with increasing severity.

- Parameter M indicates the presence of distant metastases and can be 0 (no metastases) or 1 (presence of metastases).

- A further parameter G taking values from 1 to 4, indicates the degree of differentiation of malignant cells, that is, to what extent they have maintained the characteristics of the cells from which they originated.

An X value may also be assigned to the first three parameters to indicate the inability to define that characteristic. For sentinel lymph node biopsy (SLNB Sentinel lymph node biopsy) the general orientation is to reserve the method to women with monocentric T1-T2 breast neoplasms less than 3 centimeters in diameter and with clinically negative axillary lymph nodes [13,14]. This aspect can be detected by an ultrasound of the axillary cavity, which is able to highlight the presence of lymphadenopathy; however, this method is very operator-dependent because its outcome is related to the experience of those who perform the examination. In case of structural alterations or doubtful results, a cell sample is taken and subjected to histological examination to identify its nature. This sampling is called ultrasound-guided cytology if it is performed by ultrasound-guided needle aspiration (FNAC fine needle aspiration cytology), which involves the sampling of a few cells through a fine needle; if one or more pieces of tissue are taken through a thicker needle it is called biopsy and can be performed under ultrasound guidance (CB Core Biopsy) or under stereotactic mammographic guidance (Mammotome).

Excellent results over the years, have made it possible to select even cases of multifocal neoplasms but only if the overall diameter of the foci is less than 3 cm and always with clinically negative axillary lymph nodes; multifocality of a neoplasm means the presence of multiple foci in the same breast quadrant.

Patients undergoing conservative surgery with sentinel node biopsy should undergo standard follow-up, i.e., with a visit initially every six months, and with annual mammography. The periodic examination should include an accurate clinical examination of axillary lymphoglandular stations; if one or more lymph nodes are found to be enlarged, an axillary ultrasound and a possible needle aspiration may be useful. In case of recurrence of disease in the axilla (3-4% of cases), it is necessary to resort to delayed complete axillary lymphadenectomy[14,15].

In cases where the sentinel lymph node is positive on histological examination, axillary dissection is performed; in order to reduce motor limitations of the upper limb, cycles of physiotherapy can be performed.

In cases where the sentinel lymph node is negative, adjuvant radiation therapy is used to reduce the probability of local recurrence of the tumor.

As mentioned, several times, the sentinel node technique allows to reduce the incidence of upper limb lymphedema, compared to complete axillary dissection. However, it should be noted that the incidence of lymphedema after delayed lymphadenectomy, due to false-negative sentinel nodes or to recurrence of disease in the axilla, is about 17% higher than after primary lymphadenectomy, probably because an area already surgically manipulated is re-operated [15].

5. Conclusions

Axillary lymph node status still remains the most important prognostic factor in malignant breast neoplasia. Selective sentinel lymph node (LS) biopsy was developed to assess axillary lymph node status and avoid unnecessary surgery (axillary lymphadenectomy) in patients with histologically negative lymph nodes for metastases. At present, ALND is performed in all cases of positive LS, although some studies raise the debate whether to perform it in patients with micrometastases and isolated tumor cells.

The most widely used technique for LS individualization is the one using radioactive tracer (99mTc), which has a high accuracy and a very low probability of false negative results. Compared to an ALND, this technique involves fewer complications for the patient (lymphedema, motor deficits, etc.), lower costs and execution times, saving of immunocompetent tissue and a psycho-physical improvement of the woman. The main disadvantage is the compulsory presence of a nuclear medicine service to perform lymphoscintigraphy and produce the radiopharmaceutical; another disadvantage is the exposure to ionizing radiation, although minimal, that the use of radioisotope involves.

The method with the magnetic tracer is a valid alternative to the use of radioactive tracer, especially for those hospitals that do not have a nuclear medicine section; it allows an enormous reduction in costs and time by avoiding the scintigraphic procedure before and during the operation. It also avoids all the disposal procedures of materials contaminated by radioactive substance and the compulsory closure times of the operating room required by law. This method does not imply a loss of information since the scintigraphic examination can be replaced by the one with magnetic detector; in this way there will be a complete elimination of the exposure to ionizing radiation both of the health team and of the patient. This will also reduce the time required for the patient's diagnostic procedure, thus decreasing his psychological stress, which is already of considerable importance, since he is faced with a malignant pathology.

Funding: This research received no external funding.

Author Contributions: conceptualization, I.P, S.S, and C-P.M.; methodology, I.S., and M.D.; validation, I.L. and I.P.; formal analysis, P.A. and I.S.; investigation, B.L.; resources, I.L.; data curation, G.R.; writing—original draft preparation, I.P; writing—review and editing, I.P.; visualization, G.G.; supervision, G.G.; project administration, I.L.; funding acquisition, P.A. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Sapienza University Research Federated Athensis n. C26F09B5E5.

Informed Consent Statement: Patient consent was waived due to the retrospective study design.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: All other authors have nothing to disclose.

References

1. https://www.senologia.it/collegio-dei-senologi/linee-guida-e-documenti/
2. https://www.aiom.it/linee-guida-aiom-2021-neoplasie-della-mammella/
3. Cserni G, Maguire A, Bianchi S, Ryska A, Kovács A. Sentinel lymph node assessment in breast cancer-an update on current recommendations. Virchows Arch. 2021;10.1007/s00428-021-03128-z. doi:10.1007/s00428-021-03128-z
4. Galimberti V, Cole BF, Zurrida S, et al. Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial [published correction appears in Lancet Oncol. 2013 Jun;14(7):e254]. Lancet Oncol. 2013;14(4):297-305. doi:10.1016/S1470-2045(13)70035-4
5. Ahmed M, Purushotham AD, Douek M. Novel techniques for sentinel lymph node biopsy in breast cancer: a systematic review. Lancet Oncol. 2014;15(8):e351-e362. doi:10.1016/S1470-2045(13)70590-4

6. Shiozawa M, Lefor AT, Hozumi Y, et al. Sentinel lymph node biopsy in patients with breast cancer using superparamagnetic iron oxide and a magnetometer. Breast Cancer. 2013;20(3):223-229. doi:10.1007/s12282-011-0327-9
7. Izzo L, Messineo D, DI Cello P, et al. Correlation Between Onco-suppressors PTEN and NM23 and Clinical Outcome in Patients with T1 Breast Cancer. In Vivo. 2021;35(1):169-174. doi:10.21873/invivo.1224
8. Douek M, Klaase J, Monypenny I, et al. Sentinel node biopsy using a magnetic tracer versus standard technique: the SentiMag Multicentre Trial. Ann Surg Oncol. 2014;21(4):1237-1245. doi:10.1245/s10434-013-3379-6
9. Donker M, van Tienhoven G, Straver ME, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. Lancet Oncol. 2014;15(12):1303-1310. doi:10.1016/S1470-2045(14)70460-7
10. Christenhusz A, Pouw JJ, Simonis FFJ, et al. Breast MRI in patients after breast conserving surgery with sentinel node procedure using a superparamagnetic tracer. Eur Radiol Exp. 2022;6(1):3. Published 2022 Jan 27. doi:10.1186/s41747-021-00257-7
11. Messineo D, Izzo L, Pisanelli MC, Razionale F, Izzo S, Izzo P. The influence of preoperative MRI in early breast cancer: gold standard. Ann Ital Chir. 2020;91:144-153.
12. Deng H, Lei J, Jin L, Shi H. Diagnostic efficacy of sentinel lymph node in breast cancer under percutaneous contrast-enhanced ultrasound: An updated meta-analysis. Thorac Cancer. 2021;12(21):2849-2856. doi:10.1111/1759-7714.14139
13. Sreedhar S, Maloney J, Hudson S. Introducing SentiMag in a rural setting: a 5-year experience. ANZ J Surg. 2021;91(11):2404-2410. doi:10.1111/ans.17093
14. Yılmaz OC, Vural V. Feasibility of Magnetic Technique for Axillary Staging after Neoadjuvant Therapy in Breast Cancer Patients. J Invest Surg. 2022;1-4. doi:10.1080/08941939.2022.2038737
15. Rulli A, Covarelli P, Servoli A, et al. Accuracy and feasibility of SentiMag technique for localization of non-palpable breast lesions. Minerva Chir. 2020;75(4):255-259. doi:10.23736/S0026-4733.20.08303-0