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Methods of localisation of sentinel node biopsy for breast cancer patients - current and prospective overview

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Abstract

Background

Breast cancer is one of the most common cancers in the adult population and due to advances in screening, its numbers are increasing every year. Assessment of sentinel node is a standardized method for staging of the axillary disease in clinically and radiologically normal axilla. Most recently attempts have been made for different than traditional dual technique.

Methods

We have looked into available research and databases to explore various available options that have been trialed or that show some prospective in sentinel node localisation. Some of these showed great potential for non-invasive/minimally invasive assessment in the future.

Results

While researching this topic, there was obvious division into operative and non-operative techniques. The operative techniques were more traditional dual technique or combination/sole tracer with newer techniques such as indocyanine green or superparamagnetic iron oxide. The non-operative techniques usually showed a combination of advanced imaging with or without biopsy.

Discussion

Although the dual technique is reliable and brings results there are some promising data from both operative and non-operative techniques. While the operative options offer mainly alternatives to the dual technique while avoiding known side effects, the non-operative techniques show quite revolutionary potential. As we are already reducing the amount of surgical intervention in the axilla, this might be an area for further research and trials.

Keywords: Sentinel Node Biopsy, Breast Cancer, Prospective Overview.

Background

Breast cancer is one of the most common cancers in the adult population and due to advances in screening, its numbers are increasing every year. Assessment of sentinel node is a standardized method for staging of the axillary disease in clinically and radiologically normal axilla.

Sentinel node biopsy using "dual technique" (combination of radioisotope and blue dye) has been standard in the UK for many years. This is a well established technique that can achieve more than 90% identification rate with less than 10% false-negative rate. However due to its logistics issues, availability and adverse site effects, other methods of marking sentinel node biopsy have been explored. Worldwide single tracer method is acceptable due to the problems mentioned above. [1]

This overview is to serve as a summary of techniques currently used with some non-operative techniques that are currently being explored and may change practice completely in the future.

Methods

Thorough search of the PubMed database has been performed to summarize different methods of sentinel node biopsy marking. This has been combined with the author's own experience from panel discussion and different practice over Europe. For the purpose of this article division for operative and non-operative technique has been used, the overview is in the table below. [2]

OPERATIVE TECHNIQUES	Radioactive tracer
	Blue dye
	Combination technique ("dual method")
	Superparamagnetic iron oxide
	Fluorescence technique Indocyanine green Fluorescein
	Tattooing with sterile black carbon suspension
NON-OPERATIVE TECHNIQUES	Computer tomography lymphography
	Contrast enhanced ultrasound
	Photoacoustic imaging
	Radiomics

Results

Radioactive tracer

The most common tracer used isTcM99m. It is used as a sole agent or in combination with other methods. Whether used combined with other techniques or as a single tracer, it brings with it financial as well as logistical burden. The injection has to happen as close to surgery as possible, which means either on a day of surgery or the day before. The day before surgery means an extra trip for the patient and potentially lower signal on the probe in theatre. The day of the surgery can pose delays as most nuclear medicine departments in the UK do not open until 9 am. This on its own requires a careful theatre list planning and management. [3]

The main financial burden comes from the radioactive element of the tracer. Although it is safe to use

in the vast majority of patients, it is a radioactive compound and therefore has to be stored and managed accordingly. Not all hospitals are equipped to store radioactive material on site and rely on delivery on the day of surgery.

The biggest advantage of radioactive tracer is the fact that it could be used in almost all patients with minimal risk of adverse reaction. This is a very attractive option and even as a single agent it has good detection rates. [4]

As it is usually used in combination with other agents, further details would be discussed in the combined technique part of this article.

Blue dye

This is a well established and recognised technique. Historically methylene blue has been used, while nowadays the tendency moved to usage of Patent Blue V. It is rarely used as a single agent but works well in combination with radioactive tracer.

Usage of blue dye carries a risk of complications such as tattooing of the skin and allergic reaction which can range from rash to anaphylaxis. Unless part of a trial, the adverse reactions to blue dye are severely under-reported.

There are some differences reported in use of the blue dye itself by different surgeons in the UK. Some use the blue dye neat but use 1ml or 2ml applications. While some surgeons prefer diluted solution with normal saline or water. This can differ from using 1-2ml of blue dye and 1-9ml of solution agent. In the studies that have been conducted, there is no significant difference between diluted and undiluted blue dye. [5]

As blue dye is usually used as part of "combined technique" with radioactive tracer, it would be discussed below.

Combination technique

This technique uses both radioactive and clue dye and it is the golden standard for sentinel node biopsy. Using this combined technique has achieved identification rates of 96-97% in both AMAROS and ALMANAC trials. [6,7] It has been proven before that using the combination technique is better than using either tracer in isolation. Despite this many centres have decided to omit use of blue dye due to the related adverse risks.

Although this technique has a very high identification rate, it also combines the disadvantages of both including adverse reactions to blue dye as well as the logistic and financial burden of nuclear medicine.

Superparamagnetic iron oxide

Nanoparticles of superparamagnetic iron oxide (SPIO) have been initially used in magnetic resonance as a contract agent. Endomagnetics Ltd developed Sienna+ applied this technology which is used as tracer in sentinel node biopsies. It is user friendly with a similar sequence as blue dye. 2ml of Sienna+ is diluted to 5ml with saline and injected into the breast and massaged for 5 minutes.The sentinel node stains brown and it is detectable using hand-held Sentimag probe. This is a big advantage as it combines the visual element with a magnetometer. However a slightly longer time has to be allowed for the migration of the radioisotope - recommendations are 20 minutes. As it relies on ferromagnetic signal, it could be distorted by metal instruments and therefore plastic instruments are recommended.

The technique is contraindicated in patients with iron allergy, iron overload, pacemaker or other ferrous metal containing devices in the chest wall. [8]

The detection rate has been reported 94.4-98% by different studies and recent meta-analysis showed non inferiority of this technique to standard sentinel node detection techniques.

The tracer is not radioactive and therefore the issues connected with radioactivity of tracer are not present, however the transcutaneous detection of the probe is definitely worse than that of radioactive tracer. Its detection worsens with increased depth of the tissues. Additionally there could be brown discoloration of the skin and detectable magnetic activity which can persist for up to 5 years and distort MRI images. [9]

Fluorescence techniques

Indocyanine green (ICG)

The main use of indocyanine green is to assess liver function, cardiac output and free flap perfusion. It binds to plasma proteins and fluoresces in near-infrared wavelengths. When injected as blue dye (intra or subdermally into the retroareolar region), it could be visualised in the axilla to help and determine sentinel nodes. It requires a special equipment camera as it is not visible to the naked eye. This increases the cost of the procedure and therefore is usually used in the centres where ICG and the cameras are used for other purposes. [10]

In our unit, the main downfall of this otherwise quite slick technique was that you need an extra pair of hands to hold the camera or you are constantly switching between operating and scanning. The other disadvantage is that disruption of lymphatics can lead to leakage of ICG into the wound which makes identification of sentinel node very difficult. The ICG cannot be used in patients with iodine allergy as it contains sodium iodide.

It appears a very simple and efficient method however there is lack of evidence comparing this to the standard technique.

Fluorescein

Fluorescein is a low cost dye that has initially found its use in ophthalmology and neurosurgery. Its 10% solution is widely available and a blue light source is needed to excite fluorescence. It is described in sentinel node mapping for colorectal tumours. A single randomised trial has been conducted and their interim analysis showed promising data in similar detection rates to the standard combined technique. This appears to be a promising low cost option that could be available in developing countries, however the evidence is limited. [11]

Tattooing with sterile black carbon suspension

Tattooing of sentinel nodes or tumours is an old technique that is still widely used. It uses suspended carbon particles and can get injected straight after code biopsy not only into the node but can be used to fill the biopsy tract to help and guide surgeons during the operation. It results in black staining to the node and the tract. However it is not visible on any imaging and therefore relies on correct placement in the first attempt. It is an effective and low cost technique which is in some countries used in combination with blue day or radioactive tracer. It could be used as marking prior to neoadjuvant chemotherapy with no disturbance of imaging that is used to monitor progress, especially MRI. [12]

It is also well seen on pathological slides and therefore can help further confirmation of correct node

sampling.

It cannot be used as sentinel node tracer as such but has great advantages in marking nodes for targeted axillary dissection.

Although sentinel node biopsy is minimally invasive as compared to axillary clearance, it is still associated with some risk and adverse reaction to the tracer being used. More recently, trials challenging the need for any axillary treatment in patients with minimal disease in the axilla, have been conducted. It could raise the question whether there is a role for sentinel node biopsy in the future. Some of the efforts of research have been redirected towards non surgical assessment of the axilla.

Computed tomography lymphography (CTLG)

This method has been mainly used in Japan. It uses a combination of blue dye or IGC with 3D CTLG. It has been done 1 day prior to surgery by injecting the tracer as usual, proceeding to CT shortly after. 3D CT images are then reconstructed to show lymphatics and sentinel nodes. These could be marked on the skin using a laser navigator system.

It has been noted that there is a high chance of metastasis when the images showed not stained or poorly stained sentinel nodes or blocked lymphatics. This could be explained by replacement of tissue with cancer cells.

The detection rate of sentinel node is really high (98-100%) for sentinel node biopsy, however the CTLG alone has high false negative rates of metastases. [13]

This is a promising technique however it does not take the pressure of logistics from the radiology department. Furthermore it exposes patients to radiation from CT itself. It is difficult to see this method replacing the established combined techniques but there is definitely scope for future work.

Contrast enhanced ultrasound (CEUS)

This method combines the use of ultrasound contrast agent with specific mode on the machine. It can obtain CEUS images to help identify sentinel node. The second generation of contrast agents uses microbubbles of various gases within a shell. Once the microbubble is destroyed, the gas is released and can be identified by the machine. The gases are inert and do not interfere with the body, however the shell can be regarded as foreign material by the immune system and cause hypersensitivity.

The contrast is injected similar to the other agents into the retroareolar region and massaged to the breast. US is used shortly following this mapping the lymphatics and sentinel node. This could be used for percutaneous sampling of the sentinel node to try and avoid biopsy all together.

The detection rate of CEUS ranges from 70 to 100% in various studies.[14] There is a high false negative rate reported in some of the studies. Despite that the CEUS has a good potential and has several advantages including no radiation and no effect on renal or thyroid function.

Photoacoustic imaging (PAI)

This type of imaging has been attracting a lot of interest due to its potential. It uses an optical beam inducing vibration and rotational oscillation of a particular wavelength. This leads to delivered energy being converted to heat and thermoelastic ex-

pansion that generates acoustic waves. The frequency of the wave is in the ultrasonic range and therefore could be detected by the US. Images can be used as microscopy, tomography or cross sectional depending on the detection scheme and can be watched in real time. The most used application is measurement of oxygen saturation.[15]

Blue dye and ICG could be used as agents for PAI and they differ in the depth of the tissue. Other magenta have been assessed such as gold based particles or carbon nanotubes conjugated with ICG. Some attempts have been made to perform PAI without agent to lessen the burden on clinicians and patients.

Some studies have shown good results from the combination of PAI with other traditional imaging, such as the US. This can lead to exploited images to visualise the accumulation of contrast.

Using PAI can help identify sentinel node and facilitate image guided biopsy pre-operatively.

There is clearly a great scope for exploration in the future.

Radiomics

Radiomics uses models based on dynamic contrast-enhanced MRI (DCE-MRI). Recent studies have shown that there is good performance in prediction of metastases using these models. These models have different performance in prediction but they are all showing good initial results. [16] This is a quickly evolving area of medicine that will definitely play some major part in the future.

Discussion

Sentinel node biopsy has without the doubt changed the management of breast cancer. The newer techniques are reactions to already reported adverse reactions and complications or other issues that we have encountered over the years (financial or logistical). It is further supported by recent trials that show that we should try and minimize the surgical interventions in the axilla.

A common hurdle to try and establish a new method is lack of good quality of evidence. We are missing randomised controlled trials or cost-effectiveness studies. Some of these techniques are going to be even less achievable in the low income countries due to their costs and availability.

There is definitely a shift in the operative approach to the axilla. There is increasing interest in non-operative assessment. A lot of the techniques we have mentioned have great potential but would require future development and re-evaluation.

References

1. Veronesi, U. · Paganelli, G. · Viale, G. et al., A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer, N Engl J Med. 2003; 349:546-553
2. Kurosumi M. Recent trends concerning sentinel lymph node biopsy for breast cancer and new methods for detection of metastasis. Breast Cancer. 2007;14(4):341. doi: 10.2325/jbcs.14.341. PMID: 17986797.
3. Xu L, Yang J, Du Z, Liang F, Xie Y, Long Q, Chen J, Zeng H, Lv Q. Redefining Criteria to Ensure Adequate Sentinel Lymph Node Biopsy With Dual Tracer for Breast Cancer. Front Oncol. 2020 Dec 3;10:588067. doi: 10.3389/fonc.2020.588067. PMID: 33344240; PMCID: PMC7744718.
4. Bove S, Fragomeni SM, Romito A, DI Giorgio

D, Rinaldi P, Pagliara D, Verri D, Romito I, Paris I, Tagliaferri L, Marazzi F, Visconti G, Franceschini G, Masetti R, Garganese G. Techniques for sentinel node biopsy in breast cancer. Minerva Surg. 2021 Dec;76(6):550-563. doi: 10.23736/S2724-5691.21.09002-X. Epub 2021 Aug 2. PMID: 34338468.

5. Li J, Chen X, Qi M, Li Y. Sentinel lymph node biopsy mapped with methylene blue dye alone in patients with breast cancer: A systematic review and meta-analysis. PLoS One. 2018 Sep 20;13(9):e0204364. doi: 10.1371/journal.pone.0204364. PMID: 30235340; PMCID: PMC6147575.
6. Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJ, Mansel RE, Cataliotti L, Westenberg AH, Klinkenbijl JH, Orzalesi L, Bouma WH, van der Mijle HC, Nieuwenhuijzen GA, Veltkamp SC, Slaets L, Duez NJ, de Graaf PW, van Dalen T, Marinelli A, Rijna H, Snoj M, Bundred NJ, Merkus JW, Belkacemi Y, Petignat P, Schinagl DA, Coens C, Messina CG, Bogaerts J, Rutgers EJ. 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 Nov;15(12):1303-10. doi: 10.1016/S1470-2045(14)70460-7. Epub 2014 Oct 15. PMID: 25439688; PMCID: PMC4291166.
7. Mansel RE, Fallowfield L, Kissin M, Goyal A, Newcombe RG, Dixon JM, Yiangou C, Horgan K, Bundred N, Monypenny I, England D, Sibbering M, Abdullah TI, Barr L, Chetty U, Sinnett DH, Fleissig A, Clarke D, Ell PJ. Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC Trial. J Natl Cancer Inst. 2006 May 3;98(9):599-609. doi: 10.1093/jnci/djj158. Erratum in: J Natl Cancer Inst. 2006 Jun 21;98(12):876. PMID: 16670385.
8. Kurylcio A, Pelc Z, Skórzewska M, Rawicz-Pruszyński K, Mlak R, Gęca K, Sędłak K, Kurylcio P, Małecka-Massalska T, Polkowski W. Superparamagnetic Iron Oxide for Identifying Sentinel Lymph Node in Breast Cancer after Neoadjuvant Chemotherapy: Feasibility Study. J Clin Med. 2021 Jul 16;10(14):3149. doi: 10.3390/jcm10143149. PMID: 34300315; PMCID: PMC8305632.
9. Chapman MC, Lee AY, Hayward JH, Joe BN, Price ER. Superparamagnetic Iron Oxide Sentinel Node Tracer Injection: Effects on Breast MRI Quality. J Breast Imaging. 2020 Nov 21;2(6):577-582. doi: 10.1093/jbi/wbaa083. PMID: 38424862.
10. Coibion M, Olivier F, Courtois A, Maes N, Jossa V, Jerusalem G. A Randomized Prospective Non-Inferiority Trial of Sentinel Lymph Node Biopsy in Early Breast Cancer: Blue Dye Compared with Indocyanine Green Fluorescence Tracer. Cancers (Basel). 2022 Feb 10;14(4):888. doi: 10.3390/cancers14040888. PMID: 35205636; PMCID: PMC8870473.
11. Yadav SK, Bharath S, Sharma D, Srivastava A, Jha CK, Agarwal G, Khadka S, Singh M, Shekhar S, Goyal A. A systematic review and meta-analysis of diagnostic performance of fluorescein-guided sentinel lymph node biopsy in early breast cancer. Breast Cancer Res Treat. 2024 Jul;206(1):19-30. doi: 10.1007/s10549-024-07310-0. Epub 2024 Apr 26. PMID: 38668856.
12. Natsiopoulos I, Intzes S, Liappis T, Zarampoukas K, Zarampoukas T, Zacharopoulou V, Papazisis K. Axillary Lymph Node Tattooing and Targeted Axillary Dissection in Breast Cancer Patients Who Presented as cN+ Before Neo-

adjuvant Chemotherapy and Became cN0 After Treatment. Clin Breast Cancer. 2019 Jun;19 (3):208-215. doi: 10.1016/j.clbc.2019.01.013. Epub 2019 Feb 6. PMID: 30922804.

13. Kamata A, Miyamae T, Koizumi M, Kohei H, Sarukawa H, Nemoto H, Hino K. Using Computed Tomography Lymphography for Mapping of Sentinel Lymph Nodes in Patients with Breast Cancer. J Clin Imaging Sci. 2021 Aug 14;11:43. doi: 10.25259/JCIS_33_2021. PMID: 34513207; PMCID: PMC8422530.
14. Machado P, Liu JB, Needleman L, Lazar M, Willis AI, Brill K, Nazarian S, Berger A, Forsberg F. Sentinel Lymph Node Identification in Patients With Breast Cancer Using Lymphosonography. Ultrasound Med Biol. 2023 Feb;49(2):616-625. doi: 10.1016/j.ultrasmedbio.2022.10.020. Epub 2022 Nov 26. PMID: 36446688; PMCID: PMC9943072.
15. Liu S, Wang H, Zhang C, Dong J, Liu S, Xu R, Tian C. In Vivo Photoacoustic Sentinel Lymph Node Imaging Using Clinically-Approved Carbon Nanoparticles. IEEE Trans Biomed Eng. 2020 Jul;67(7):2033-2042. doi: 10.1109/TBME.2019.2953743. Epub 2019 Nov 15. PMID: 31751215.
16. Yu Y, Tan Y, Xie C, Hu Q, Ouyang J, Chen Y, Gu Y, Li A, Lu N, He Z, Yang Y, Chen K, Ma J, Li C, Ma M, Li X, Zhang R, Zhong H, Ou Q, Zhang Y, He Y, Li G, Wu Z, Su F, Song E, Yao H. Development and Validation of a Preoperative Magnetic Resonance Imaging Radiomics-Based Signature to Predict Axillary Lymph Node Metastasis and Disease-Free Survival in Patients With Early-Stage Breast Cancer. JAMA Netw Open. 2020 Dec 1;3(12):e2028086. doi: 10.1001/jamanetworkopen.2020.28086. PMID: 33289845; PMCID: PMC7724560.