**SentiMag® and Sienna+® system for sentinel lymph node biopsy in breast cancer**

**SUMMARY**

The SentiMag® and Sienna+® system is intended to be used in breast cancer surgery to help a surgeon to identify the lymph nodes most likely to be affected if the cancer has spread. It consists of a hand-held probe, which detects magnetism, the SentiMag®, and a magnetic tracer, Sienna+. The lymph nodes it identifies can be removed and examined to help assess the stage of the disease and how best to treat it. Sienna+® is injected into the affected breast then flows through the lymphatic system and becomes trapped in nearby lymph nodes. During surgery the SentiMag® probe is used to find these nodes. The system may offer an alternative to using a radioactive tracer to help find the nodes, which is the current practice. More research is needed before it is known how this new system compares to this current technique for identifying the nodes.

**BACKGROUND**

Breast cancer starts with genetic changes in a single cell or small group of cells in the breast. These changes allow cells to reproduce uncontrollably, creating a tumour. Cells from the tumour can then spread to other sites in the body via the lymphatic system or the bloodstream.

The lymphatic system is a system of thin tubes running throughout the body which drain fluid from the tissues back into the bloodstream. Along the lymphatic system are small glands called lymph nodes. If breast cancer spreads, it is usually first to lymph nodes located under the arm (the axillary lymph nodes). The sentinel lymph node is the node that lymph from the breast drains through first. The presence or absence of cancer in this lymph node is an indicator of the disease stage and outlook and this information is important in planning treatment. Removal of lymph nodes to
which cancer has spread is also important to prevent the disease returning\(^1\).

Breast cancer is the most common cancer in the UK and accounts for 31% of all new cases of cancer among women. Breast cancer incidence is strongly related to age, with the highest incidence rates overall being in older women\(^2\). In England and Wales in 2007, there were 44,343 cases of breast cancer diagnosed in women\(^3\). In the UK in 2007, 82% of women diagnosed with breast cancer had surgery. Of these, 57% had a breast conserving procedure and the remaining 43% had a mastectomy (breast removal)\(^3\).

In women undergoing surgery to treat breast cancer a procedure called a sentinel lymph node biopsy (SLNB) can be performed at the same time to find out if the cancer has spread to the lymph nodes under the arm. In England and Wales in 2007, 32% of women with surgically treated breast cancer had a SLNB recorded\(^3\). This equates to approximately 11,600 women in England and Wales having a SLNB during breast cancer surgery in 2007. However, the proportion of women having SLNB during surgery has increased over time and one expert states that the percentage of SLNB during surgery in their practice is now well over 50%. Association of Breast Surgery guidelines suggest annually 25,000 to 30,000 new breast cancers a year in the UK may be suitable for SLNB\(^4\).

### CURRENT PRACTICE

The National Institute for Health and Clinical Excellence (NICE) recommends that, prior to breast cancer surgery, a clinical and ultrasound examination of the under arm is carried out to check for abnormal lymph nodes and that if abnormal nodes are identified these should be tested for tumours. If these tests show the cancer has spread to the lymph nodes, complete removal of all the nodes during surgery is recommended. However, if clinical and ultrasound examination finds no evidence that the cancer has spread to the lymph nodes a sample of lymph nodes may be removed during surgery for testing. SLNB is the preferred technique\(^5\).

During SLNB the sentinel lymph nodes are identified and removed. There may be one or more of these nodes. The sentinel lymph nodes are then examined to see if there is any cancer present. Some hospitals examine the nodes whilst the surgery is in progress, which may avoid a second operation to remove the lymph nodes should cancer be found.

To find the sentinel nodes a radioactive tracer (sulphur colloid tagged with the radionuclide technetium-99m; \(\text{\textsuperscript{99m}}\text{Tc}\)) is used to trace the lymph drainage of the breast. A minimum of 30 minutes before surgery a small amount of the radioactive tracer is injected into the affected breast. The tracer is carried to the sentinel lymph nodes by the lymphatic system. The nodes containing the radioactive tracer are found during surgery using a hand-held probe that detects radiation (a gamma probe) and are then removed for examination. The radioactive tracer is often used in combination with a blue dye which helps the surgeon identify the nodes visually. Because the tracer is radioactive the injection is normally carried out in a nuclear medicine department.

One expert comments that in hospitals without a nuclear medicine department, sampling of lymph nodes may be guided using blue dye.

### NEW TECHNOLOGY

Endomagnetics Ltd’s SentiMag\(^\circledast\) and Sienna+\(^\circledast\) system is intended to help a surgeon locate sentinel lymph nodes during breast cancer surgery. The system consists of a handheld probe, the SentiMag\(^\circledast\), and a tracer, Sienna+\(^\circledast\). The Sienna+\(^\circledast\) tracer is a dark brown liquid
containing a solution of magnetic iron oxide particles. An injection of 2ml of Sienna+® is made into the breast following anaesthesia. The magnetic particles are then absorbed into lymph capillaries and become trapped in the sentinel lymph node or nodes. The SentiMag® probe is used during the operation to detect the tracer trapped in the lymph nodes and guide a surgeon to remove them for analysis. The company state the SentiMag® probe can be used to identify sentinel lymph nodes a minimum of 30 minutes after the injection of Sienna+®. Sienna+® serves both as a magnetic marker and a visual dye (due to the dark colour of the particles). The surgeon identifies the sentinel lymph nodes by both audio and visual cues – increasing frequency and higher numbers indicate Sienna+® presence. The system is intended to replace the current technique of using a radioactive tracer (99mTc) detected with a hand-held gamma probe (often used in combination with blue dye). Sienna+® can be stored between 5ºC and 30ºC.

The SentiMag® probe was CE marked in December 2010 and the Sienna+® tracer was CE marked in December 2011. The company state that the system will be available in the UK by the end of 2012 and that launch with a partner will be announced by January 2013. They also state that the capital costs of the system will be equivalent to currently available techniques.

The system is also being researched for SLNB in colorectal cancer and melanoma.

### CLINICAL STUDIES AND RESEARCH QUESTIONS

There are no published studies of the SentiMag® and Sienna+® system for SLNB in breast cancer. Early studies were conducted using the SentiMag® probe with Feridex®, a magnetic contrast agent which is no longer manufactured. There is an ongoing study which is comparing SLNB using the SentiMag® and Sienna+® system to SLNB using a radioactive tracer and blue dye, or radioactive tracer alone, detected by a gamma probe. Some details of this study are given here.

A non-randomised study comparing the SentiMag® and Sienna+® system with the standard technique (patent blue dye and radioisotope; or radioisotope alone) for SLNB is ongoing. The target number of patients is 176 and the study is being conducted at six UK sites and one in Holland. Participants are patients with breast cancer scheduled for SLNB and who clinically and radiologically have no signs of lymph node involvement. A pre- and post-contrast magnetic resonance imaging (MRI) scan of the armpit will be made. The main outcomes that will be measured are the proportion of sentinel lymph nodes detected (detection rate) with either the standard or the new technique and the accuracy of MRI (with magnetic tracer) for the localisation of sentinel lymph nodes. In addition a cost-effectiveness analysis will be undertaken of using SentiMag® with pre-operative MRI.

### POTENTIAL IMPACT

Improving outcomes for people with cancer is a Government policy priority area.

If the results of studies using the SentiMag® and Sienna+® system show it works as well as the current system, it may offer a useful alternative technique for SLNB which does not involve the use of radioactive materials. This may be of benefit in a number of ways.

Currently, not all hospitals have nuclear medicine departments and some may not be set up to handle radioactive materials with all the strict regulations and protocols relating to their handling, transport and disposal. This leads to variation in practice between hospitals
depending upon their facilities. The SentiMag® and Sienna+® system would allow SLNB to be performed in all hospitals removing the possible need for women to travel with the delays that might involve, or to receive the more extensive surgery associated with removing all the lymph nodes.

Some women and some hospital staff are worried about the exposure to radioactivity during current methods of SLNB. While experts feel this is not a significant risk, the SentiMag® and Sienna+® system provides an option with no risk of radioactivity.

Molybdenum-99 or 99m, the radioactive component of the tracer which is currently used in SLNBs is made in just a few nuclear reactors worldwide. In the past there have been problems in achieving a consistent supply\textsuperscript{11} and one expert suggests this may occur again in the future. An alternative which does not rely upon such availability will be valuable in these situations.

A further potential benefit of the SentiMag® and Sienna+® system is that the injection can be given in the operating theatre after anaesthesia unlike the current system where the injection is given some time before anaesthesia. This may mean less discomfort for the patient.

It has not been possible to compare the costs of the SentiMag® and Sienna+® system with current practice. A review and economic evaluation of positron emission tomography (PET) and MRI for lymph node assessment in breast cancer was not able to identify a separate cost for SLNB\textsuperscript{1} and cost information for the SentiMag® and Sienna+® system was not available for this briefing. If the system allows the SLNB procedure to be performed more widely this may in some cases avoid complete lymph node removal which is a more invasive procedure, takes longer and is associated with more complications, a longer hospital stay and long-term adverse effects\textsuperscript{1}. The above factors may result in savings for the health service if the SentiMag® and Sienna+® system is used but these would need to be balanced against the cost of the SentiMag® probe and the ongoing costs of the Sienna+® tracer.

One expert comments that the use of this new system, if it is proven to be effective, may allow all hospitals to undertake best practice in SLNB, whether or not they have access to nuclear medicine facilities.

**Lay summary**

The SentiMag® and Sienna+® system is intended to be used during a breast cancer operation to identify the glands which are most likely to be affected if the cancer has spread. The system consists of a hand-held probe, the SentiMag®, and a magnetic liquid, Sienna+. Sienna+® is first injected into the breast and then some time is allowed for it to flow through the natural channels which drain from the breast and to become trapped in glands under the arm pit. The SentiMag® probe, which detects magnetism, is used during the operation to find glands where Sienna+® is trapped. These glands can then be removed and tested for cancer. Currently a radioactive substance is used for this procedure and using the SentiMag® and Sienna+® system may avoid this. More research is needed before we know how this new system compares to the current way of identifying these glands.
REFERENCES

1 Cooper K, Meng Y, Harnan S et al. Positron emission tomography (PET) and magnetic resonance imaging (MRI) for the assessment of axillary lymph node metastases in early breast cancer: Systematic review and economic evaluation. Health Technology Assessment 2011;15 (4).


