Chasing cancer with a flash of light

Elastic scattering spectroscopy and nanotechnology for breast cancer detection

Keywords
Breast Cancer • Sentinel lymph node biopsy
Elastic scattering spectroscopy • Quantum dots

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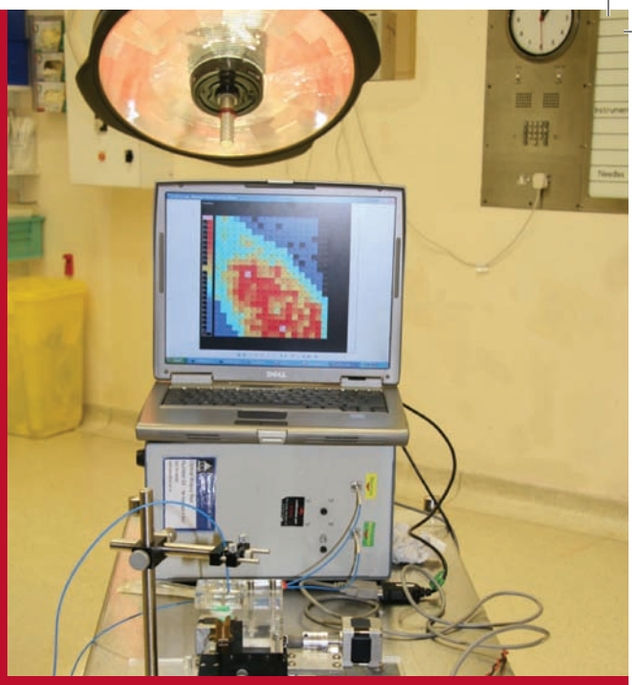
Breast cancer affects over 45,000 women in the United Kingdom. This cancer usually starts in the lining of the breast ducts and can then spread to the lymph glands in the armpit.

The first lymph gland or node under the armpit that the cancer spreads to is called the 'Sentinel Lymph Node (SLN)'. The detection of the spread of the cancer to the SLN is very important as it determines the long term survival and guides doctors in the further management of their patients. Current evidence confirms that, if the SLN is not involved with cancer, then it is highly unlikely that the rest of the lymph glands in the armpit are involved. Prior to the concept of SLN biopsy, all breast cancer patients underwent routine removal of all the glands in their armpit, with the majority of them not requiring this extensive operation and some of them suffering from the lifelong distressing symptom of lymphoedema (swelling of the arm).

Currently, the lymph glands in the armpit are removed only if we can prove that the SLN contains significant tumour deposits. This is done by a procedure called 'sentinel node biopsy' wherein one or two lymph nodes are removed by the surgeon after identifying them using radioactive and blue dyes. If cancer in the SLN can be detected during surgery, a second operation to remove the remaining lymph nodes can be avoided and reduce the physical and psychological trauma of second operations. Additionally, it would offer significant cost saving advantages to the instituition offering this diagnostic test, as the need for readmission and a second operation theatre session is prevented.



Optical Scanner set up in the operating theatre. Real time diagnosis made from the spectra obtained (as seen on the laptop screen)

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We have developed and tested a proof of principle prototype optical scanner using flashes of white light to achieve this. We use a novel optical biopsy technique called Elastic Scattering spectroscopy (ESS) which utilises pulses of white light for diagnoses of cancer. ESS uses differential light absorption and scattering properties to detect changes which occur in cancer at a cellular level. Statistical analysis allows the real-time diagnosis of the collected spectra within a short period of time in the operating theatre.

The advantages of this technique compared to other available techniques are:

- minimal running costs
- no tissue preparation or destruction
- an objective and instantaneous result; and
- no requirement for any expert personnel for interpretation, as the result is generated by a computer

We use the same technology to detect cancer within the lining of the breast duct by passing a miniature telescope through the nipple ducts into the breast. Early cancerous changes can be detected in this way long before they can be detected by x-ray or ultrasound scans or other imaging techniques. We have custom built a miniature telescope that can adopt our optical probe and allow us to perform the optical biopsy of the breast lining using ESS.

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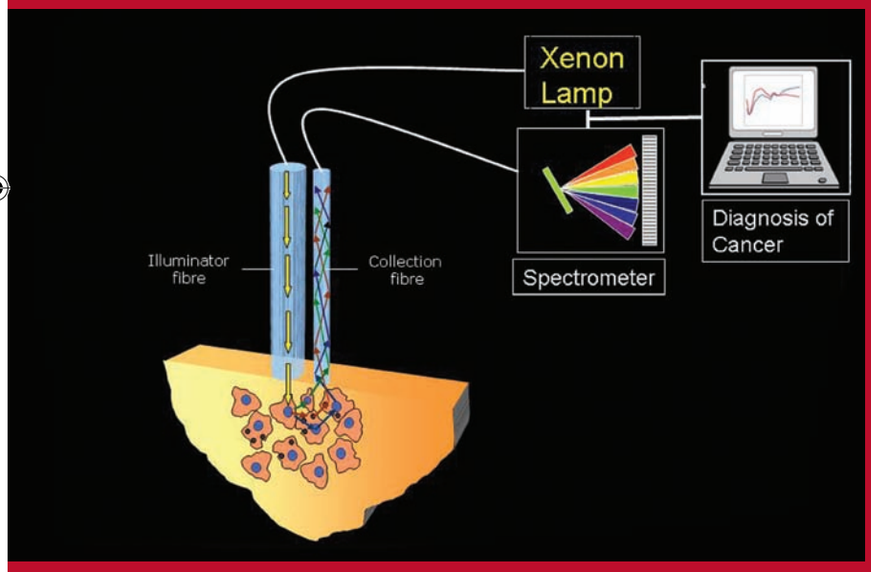
This technology has potential universal availability for real time immediate detection of other pre-cancer/cancer in other organs including – oesophageal cancer, skin cancer, cancer of the oral cavity and lung cancer.

Detection of the SLN requires the use of radioactive material which is not available in all institutions and is tightly regulated by strict policies and guidelines. To overcome this, we are developing *nanotechnology quantum dots* which are tiny fluorescent particles, to locate the key lymph gland draining breast cancer. Quantum dot (QD) nanocrystals, rendered biocompatable by a special polymer developed by our team, can be injected into the breast adjacent to the cancer. These enter the lymphatic channels and accumulate within the SLN and fluoresce on visible light illumination, enabling the surgeon to rapidly locate and remove the node without a need for radioactive tracers.

Optical Scanner set up in the operating theatre.



Schematic representation of optical biopsy device utilising Elastic Scattering Spectroscopy

In addition to the detection and diagnosis of cancer, our team is extending the use of optical technology for treatment of cancer by a procedure called photodynamic therapy (PDT). PDT uses laser, or other light sources, combined with a light-sensitive drug (called a photosensitiser) to destroy cancer cells. A photosensitising agent is a drug that makes cells more sensitive to light. Once in the body, the drug is attracted to cancer cells. When the light is directed at the area of the cancer, the drug is activated and the cancer cells are destroyed.

Further information

Website – **www.sentinelnode.net**

References:

1) Johnson K.S., Chicken D.W., Pickard D.C., Lee A.C., Briggs G, Falzon M., Bigio I.J., Keshtgar M.R., Bown S.G. Elastic scattering spectroscopy for intraoperative determination of sentinel lymph node status in the breast. *J Biomed Opt*. 2004 Nov-Dec; 9(6):1122-8.
This paper shows that ESS can identify cancer areas in lymph nodes with a high level of specificity. A publication on the ESS scanner is currently in preparation.

2) Iga AM, Robertson JH, Winslet MC, Seifalian AM. Clinical potential of quantum dots. *J Biomed.Biotechnol*. 2007:76087.
This manuscript describes the potential of Quantum Dots as markers for lymph nodes

3) Lovat L.B., Johnson K., Mackenzie G.D., Clark B.R., Novelli M.R., Davies S., O'Donovan M., Selvasekar C., Thorpe S.M., Pickard C.D.O., Fitzgerald, R.C., Fearn T., Bigio I.J., Bown S.G. (2006) Elastic scattering spectroscopy accurately detects high grade dysplasia and cancer in Barrett's oesophagus. *Gut*; 55: 1078-83.
This paper shows how ESS can be used in vivo to detect areas of high grade dysplasia in Barrett's oesophagus with a high level of sensitivity and an extremely high negative predictive value (ie if no abnormality is detected, the patient is at very low risk of developing cancer).

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