LYMPHOSCINTOGRAPHY AND LYMPHOBIOPSY FOR BREAST CANCER AND MELANOMA: ABSTRACT OF NINE YEARS OF RESEARCH

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BACKGROUND AND METHODS

Our experience took us to be part of more than 100 cases from the injection in nuclear medicine, to surgery, and finally pathology. Furthermore, we have received more than 500 study cases supplied by surgeons. Clinical trials have been conducted in almost every country utilising these techniques. I am confident that I understand how this technique should work properly and also there are several constants that we must take into consideration for breast, melanoma and other applications:

1) choosing the right patient
2) colloid type that will be used
3) activity and volume of Tc-99m
4) the time between injection and surgery vs. activity
5) a lymphoscintogram which clearly defines the patient lymphatic involved
6) use of patent blue in surgery
7) use of a surgical radiation probe properly calibrated and tested prior to surgery

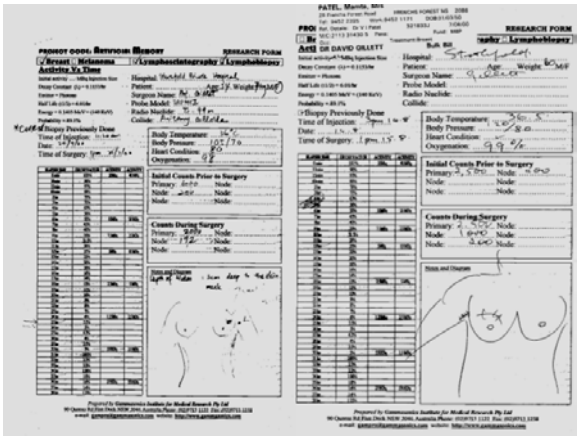

Figure 1. Sample of Research Form.

RESULTS

Lymphoscintigraphy is the study utilising an injection of a radioisotope and a colloid on the lesion site to show any lymphatic involvement between tumour and nodes.

Sentinel node. There have been many definitions written about this. Some are clear but others are totally confusing. The definition that we prefer is that "a sentinel node is any node which receives direct drainage from the lesion site".

Sometimes during lymphoscintigraphy for breast cancer, we can see clearly the movement of radionuclide into the direction of the lymphatic area or nodes. The tracer stops then re-appears a few millimeters further up, sometimes in the same direction, but in most of the cases not thus terminating at a node which normally is labelled as the sentinel node. Our study in surgery gave us a better understanding of what actually happens. * *We continue with this in lymphobiopsy.*

Lymphobiopsy is the sampling or removal of nodes in surgery labelled by radio-colloid or patent blue as sentinel nodes and confirmed by pathology.

If we take one step back, the aim of lymphobiopsy is not to find nodes with cancer or metastases. It is totally for the well being of the patient. The procedure aims to reduce invasive surgery such as axilla dissection. As this procedure normally carries complications for the life of the patient in the long term.

** In regards to the disappearance and re-appearance of the channel containing radionuclide and colloid, we have found that the radionuclide did not enter a sentinel node leaving what appears to be an empty space in the lymphoscintigram. This empty space is actually metastases blocking the entrance to the node. Normally this node are not labelled by radionuclide or patent blue and they are only millimeters apart from the node which has been labelled by the radionuclide, which is usually wrongly labelled as the sentinel node. The real sentinel node is the node which is blocked. Here is where patent blue can help. The well-trained surgeon can easily identify and see the blue channel left by the patent blue reaching a node and departing into another channel. This is not a very common occurrence, but it happens in approximately 2% of the cases.*

1. Choosing the right patients

The best patients to undergo lymphobiopsy procedures are those classified as T1 and T2. The longer the primary is in the body, the greater chance that metastases will be depleted from the primary. Most of the cases performed in Australia, UK, Europe, USA and the Western world are under the classification of T1 and T2. Pakistan, India, South East Asia and other countries, where medicine is not regulated as in the developed countries, patients do not have access to sufficient technical information to have

an early diagnosis so the majority of these cases are T3 or T4.

2. Colloid

There are several types of colloid for this procedure. The American who has brought the technique to be known to the rest of the world, are limited by FDA regulations to utilise Sulphur Colloid with the particle size varying from 50 to 2000 nm. To produce a lymphoscintogram study, they are required to filter the colloid. By performing this, approximately 70% is discarded leaving a non-uniform quantity between 15% and 30% that will finally enter the lymphatic which cannot be more than 75nm particle size. To perform surgery with the assistance of the gamma probe next day and maintain the required dose, we must inject Tc-99m between 60 and 120 MBq (and sometimes even higher) to compensate the low percentage of the colloid. Europe including the UK utilises Nano-Colloid under different names depending on the manufacturers. For example, Microlite, CisColloid, Sorin, etc. These colloids have particle sizes between 3 to 80 nm with 70% less than 10 nm. Normally we see the studies of the lymphatic showing a node during the lymphoscintogram and then disappearing. The answer to this is that due to the particle size, the compound tends to move from node to node. I also notice that the preference is for higher activity over 120MBq which I do not think is necessary.

Antimony colloid, widely used in Australia and New Zealand and introduced to neighbouring countries, has a very high percentage of uniform particle size permit studies of very high quality keeping activity low between 17 and 45 MBq, and the percentage holding the radioactive compound in the node is more reliable in surgery. In reality, I see three different techniques being treated as one and that can be confusing.

3. Activity and Volume of Tc-99m

There are three different types of injections – subdermal, intra-tumour and peri-tumour. For subdermal and peri-tumour injections, the compound tends to arrive in the same area of the lymphatic. On the other hand, by performing intra-tumour, the compound is trapped within the tumour. A new injection site in breast cancer is currently being used in the USA and Australia giving very good results which is behind the nipple.

4. Time Between Injection and Surgery VS Activity

Radioisotopes decay at a constant rate; during surgery it is critical to know the remaining activity in the patient. It was found that the optimal time occurs when the remaining activity is between 2 - 4MBq. It allows maximum performance of the Gamma Probe and adequate time for the flow of the radioisotope in the lymphatic system.

With 500 studies collected and sampling cases where between 20-40MBq was injected, it is found that the optimal times to utilise the Gamma Probe are between 14-20 hours and 20-26 hours consecutively.

5. Lymphoscintigram which Clearly Defines the Lymphatic Involved in the Patient

I strongly recommend that a lymphoscintigram must be done and properly diagnosed by Nuclear Medicine physicians prior to lymphobiopsy. The gamma probe will find nodes with or without lymphoscintigrams but greater accuracy can be achieved through understanding of the lymphoscintograms prior to the lymphobiopsy. The best results can be achieved by nuclear medicine physicians and surgeons working together closely.

6. Use of Patent Blue in Surgery

We highly recommend that patent blue be used in all surgical procedures related to sentinel node due to the rare cases of metastatic blockage, even though it is messy, expensive and can produce anomalies if the surgical procedures does not run according to schedule.

7. Use of a Surgical Radiation Probe Calibrated and Tested Prior to Surgery

All surgical radiation probes should be checked, calibrated and tested prior to every surgical procedure. Utilising a gamma probe in conjunction with radioisotope injected into patients can produce secondary problems as this is an open incision procedure where lymphatic juices carrying radionuclide can momentarily contaminate the detector giving confusing signals. Due to this we recommend that a plastic sleeve must be used even after the unit has been cleaned and sterilised. Cleaning the detector with alcohol is probably the safest way to avoid possible malfunction in the future.

One of the reasons for the incorporation of a radioactive embedded chip in the front panel of the gamma probe main unit is to develop a quality assurance system prior to surgery to confirm that the detector has not lost sensitivity after cleaning or sterilisation. Before operating the unit, counts must be taken on the check source. For increased accuracy counts should be collected and recorded daily. Any possible degradation or loss of sensitivity on the crystal can therefore be detected early and appropriate action can be taken. Otherwise, the device will find nodes in the patient but it cannot be substantiated whether it is actually finding the smallest and thus most difficult node to locate.

We see the application of lymphoscintigraphy and lymphobiopsy procedures not only in breast cancer and melanoma but also in prostate, thyroid, rectum colon and whatever there is a lymphatic connection to a lesion. In fact, 70% of female population undergoing axilla dissection do not have metastatic conditions. The removal of the lymphatic system is highly invasive producing after-effects and unnecessary mutilation to the patients. This technology is being applied to many other areas with aims to reducing the impact on patients' life, offering an alternative to radical surgery.

For those who are not aware, the Australian developed gamma surgical probe has helped more than 60,000 patients worldwide to undergo the procedures described above and has benefited dozens of students from several universities in the field of medicine, medical physics, nuclear medicine, engineering and computer science. Also it has helped to enhance a biotechnology industry and to the patients, a less morbid treatment.

Our research does not end here, we are continuously researching for less invasive and non-toxic methods with the Faculty of Biology, University of Wollongong, headed by Dr. Marie Ranson, in a project involving PAI-2. This protein labelled with an isotope has potential for future clinical use. In the near future, we will be able to label metastases by utilising this technique.

A postgraduate medical course is currently being considered and could be available through the new Faculty of Medicine at University of Wollongong.

Research also continues in the development of a Gamma Probe PC with capabilities of existing intra-cavity detection, plus real-time lymphoscintigram, artificial intelligence and voice recognition.

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