

# Radiation safety of the sentinel lymph node technique in breast cancer

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**Abstract.** Many publications attest to the potential of the sentinel lymph node technique in advancing the clinical management of melanoma and, more recently, breast cancer. Whilst not yet universally regarded as the standard of care, the technique is gaining wide acceptance. Use of a radiolabelled colloidal tracer is central to optimising sensitivity, and this brings with it the need to address radiation safety issues relating to the use of radioactive materials in the operating theatre and pathology laboratory, and the generation of radioactive waste. The radiation dose to the patient should also be determined if the professional is to reassure the patient by placing this in its proper context. For the purpose of this investigation, biodistribution data were obtained from patient studies to quantify the migration of tracer beyond the injection site, thereby permitting a detailed assessment of the internal dosimetry of the tracer and the resulting radiation dose to the patient. Uptake of tracer in the sentinel nodes, reticulo-endothelial system and circulating blood was investigated. The radiation dose to surgical staff was recorded using whole-body monitors and extremity dosimeters worn at the fingers. Clinical waste in the operating theatre was monitored and the radioactive content of significantly contaminated items determined. The radiation dose to pathology staff was estimated from knowledge of the radioactive content of the specimens obtained and a study of work practices. Migration of tracer was found to be minimal, with greater than 95% retention at the injection site. The effective dose resulting to the patient was  $2.1 \times 10^{-2}$  mSv/MBq, with a mean breast dose of  $7.2 \times 10^{-1}$  mGy/MBq. A mean whole-body dose of 0.34  $\mu$ Sv was received by surgical staff per procedure, with a mean finger dose of 0.09 mSv (90  $\mu$ Sv). Radiation doses received by pathology staff

will be predominantly below measurable levels and are likely to be negligible unless primary specimens from a large number of studies are analysed promptly upon their excision. At operation, surgical swabs can become significantly contaminated and have been found to contain up to 22% of the administered activity, dependent upon the surgical procedure performed. It is concluded that moderate activities of technetium-99m labelled tracer are administered to the patient, and the radiation risk to the patient is consequently low relative to that from many other medical exposures. The radiation doses to staff groups involved in all aspects of the technique are low, and under normal circumstances and levels of workload, routine radiation monitoring will not be required. Standard biohazard precautions prevent direct intake of radioactive contamination. Radioactive waste is created in the operating theatre, and may be generated in the pathology laboratory if specimens are not routinely stored until fully decayed. This will require special handling if the disposal of radioactive material is not permitted.

**Key words:** Sentinel lymph node technique – Intra-operative detection – Radiation safety – Radiation dosimetry – Breast cancer

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## Introduction

The sentinel lymph node technique permits the pattern of lymphatic drainage from a tumour to be investigated. Through the introduction of a suitable tracer into the immediately surrounding tissue, and by use of appropriate detection technology, these drainage routes may be identified and comprehensively mapped. Typically, this is achieved by administering a radioactively labelled colloidal material having particles within a suitable size range. The short-lived gamma-emitting radionuclide

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technetium-99m is used as a label for the colloid, and this permits images of its distribution to be obtained using a conventional gamma camera. Additionally a vital blue dye may be used as the tracer, allowing direct visual detection of the drainage path if this is sufficiently superficial to the exposed surgical field.

Whatever the form of tracer used, the sentinel lymph node technique requires that it is injected into tissue lying adjacent to the primary tumour. Its subsequent transport via the lymphatic system is then taken to reflect the functional pattern of lymphatic drainage from the tumour. The first lymph node, or nodes, demonstrating a direct uptake of tracer from the injection site are defined as sentinel lymph nodes, and are taken to act as indicator node(s) for the spread of cancer from the primary tumour site. If all such sentinel nodes are negative for tumour metastasis on histopathological examination then it has been shown that, overwhelmingly, all other lymph nodes within the same basin will also be found negative for malignancy [1].

The concept of the sentinel node was first advanced in 1977 by Ramon Cabanas [2]. In relation to penile cancer, Cabanas hypothesised the existence of a node whose histopathological status could be used to predict metastatic spread of disease, and using contrast lymphangiography he demonstrated a technique for localising the sentinel node within the inguinal lymph node basin. The sentinel node technique as we recognise it today incorporates either or both of the separate procedures of radionuclide-guided sentinel node localisation and lymphatic mapping using the blue dye, each having been developed independently of the other.

Lymphatic mapping was pioneered by Morton et al., who in 1992 [3] used a vital blue dye to visually identify lymphatic drainage paths from a primary tumour, thereby mapping the pattern of drainage. They applied the technique to the treatment of early (clinical stage I) malignant melanoma, identifying the sentinel node and submitting it to detailed histological analysis to determine those patients with nodal metastases who would benefit from radical lymphadenectomy. Lymphatic mapping was subsequently applied to the investigation of breast cancer, initially by Giuliano et al. in 1994 [4].

The technique of gamma-probe guided sentinel node localisation using radiolabelled tracers was developed by Alex and Krag, initially in a feline model [5], as an alternative approach to the use of blue dye for localisation of the initial draining lymph node. They rapidly applied the technique clinically in the investigation of both melanoma [6] and breast cancer [7]. Albertini and co-workers were the first to combine the use of both methodologies to enhance the overall sensitivity of the technique, initially applying this approach in breast cancer, where they successfully identified the sentinel lymph node in 92% of the subjects investigated [8].

Acceptance of the sentinel lymph node technique has progressed rapidly since these initial studies and it has

become regarded by some workers, at least, as the standard of care for malignant melanoma [9], although other groups highlight issues remaining to be resolved [10]. In breast cancer the technique is, as yet, less well established. With similar reservations, a number of publications report data attesting to its potential as a powerful clinical tool [11, 12], whilst others await the results of large-scale multi-centre trials to provide a more definitive answer [13, 14].

With a number of such clinical trials to evaluate the technique now in progress at centres worldwide, it seems appropriate to investigate in detail those radiation safety issues pertinent to the technique. This paper represents an attempt to meet this aim specifically for the sentinel lymph node technique applied to breast cancer.

The primary requirements of such a radiation safety assessment are to evaluate and if at all possible to quantify the level of risk ensuing to the patient so that health professionals are able to provide appropriate information and reassurance, and to provide radiation protection personnel with the data they require to implement proper precautions for staff involved at key stages of the procedure to ensure that they are not unduly exposed to sources of radiation. If radioactive waste is generated as a result of the investigation then this may also lead to a radiation exposure to the public if it is incorrectly processed at disposal, and this too must therefore be investigated. This study attempts to achieve these aims by investigating the dose and the consequent risk to: (a) the patient through administration of the tracer, (b) staff groups through their occupational exposure to the patient and/or any radioactively tagged surgical specimens and (c) the public through the creation of radioactive waste.

The absorbed radiation dose to the patient is estimated here by applying established methodologies for internal radiation dosimetry to data directly obtained from observations of the behaviour of the labelled radiocolloid subsequent to its administration, together with data relating to the physical properties of the radionuclide label itself. From the absorbed radiation dose obtained by this method further calculations may be made to estimate the "effective" radiation dose to the patient, permitting the dose received by the patient to be compared with that resulting from other forms of radiation exposure. The relative risk to the patient may also be estimated and placed in a wider context, using established assumptions drawn from available epidemiological data.

Estimates of the radiation dosimetry for conventional lymphoscintigraphy techniques have been made by a number of workers in the field, but the radiation dose arising from a sentinel lymph node investigation will differ somewhat from that obtained for these studies. Primarily this is due to the altered route of tracer administration, and the dose will differ further according to the exact anatomical site under investigation and quite possibly also in relation to the precise technique adopted for administering the tracer. Thus, radiation dosimetry for the

sentinel lymph node technique merits a specific investigation, and dosimetric estimates for the technique will need to be based upon data directly obtained from sentinel lymph node studies. Data are presented here for the technique as applied to the investigation of breast cancer.

The radiation dose received by members of staff can be determined both by direct measurement and through estimations made using published dose-rate data and observations made with regard to the duration, scheduling and nature of the exposure. Exposure to the patient or their surgical specimens may result in a radiation dose to the whole body, or to a limited region only, e.g. the hands. Thus, measurement of the radiation dose resulting to personnel should reflect their specific pattern of exposure.

In the nuclear medicine clinic, technologist staff will receive a minimal increase in their occupational exposure through imaging the sentinel node patient as the administered activity for this procedure is between one and two orders of magnitude lower than that used for the majority of nuclear medicine investigations. As designated radiation workers they will also work under local requirements for the continuous monitoring of personal radiation dose. Similarly, if the tracer is administered by a nuclear medicine professional then this will result in a minimal addition to their total dose. Consequently, nuclear medicine staff have not been addressed in this assessment of occupational exposures arising from the sentinel node procedure.

In the operating theatre, surgical staff and their assistants will receive a radiation dose to the whole body and, more significantly in some cases, to the hands. Remaining theatre personnel will receive a lesser radiation dose by virtue of their greater distance from the patient and thus, if the lead surgical staff are directly monitored, reference data are obtained from which the dose to remaining theatre staff may be inferred.

The radiation dose received by staff in the pathology laboratory will result from contact with surgical specimens containing the radioactive tracer, and thus exposure will be both to the whole body and, particularly, to the hands.

Beyond the well-regulated environment of the nuclear medicine clinic, radioactive waste may be created in both the operating theatre and the pathology laboratory. This aspect of the safety assessment was investigated through a review of work procedures in respect of their capacity to generate radioactive waste, coupled with direct radiation monitoring of the waste and measurement of the activity content for selected items.

## Materials and methods

### *Patient dosimetry*

A number of approaches have been adopted for administering the tracer by those groups currently evaluating the sentinel node tech-

nique in breast cancer. The tracer has been injected both subdermally and peritumorally, and by at least one group, intratumorally. Consequently its drainage from the administration site will be markedly more limited than is observed in conventional lymphoscintigraphy studies. Image data obtained at early time points after injection of the tracer indicate clearly that the administered radioactivity is retained initially within interstitial spaces at the injection site. Subsequent to this, biodistribution of the radiolabelled tracer will be controlled by mechanisms of transport specific to its colloidal form, where this is essentially exclusive to drainage via the lymphatic system to the reticulo-endothelial system (RES). This pattern of clearance may be indicated at later time points by discernible concentrations of tracer in the liver, spleen or bone marrow. Some minor uptake into the peripheral vascular system may also arise due to leakage of a small amount of tracer into the network of capillaries surrounding the injection site. To acquire a detailed knowledge of the nature of this subsequent biodistribution, data were gathered from gamma camera imaging, blood sampling and the gamma counting of biopsy specimens. This is detailed below, together with relevant aspects of the clinical protocol followed.

*Collection of biodistribution data.* Data were obtained from sentinel lymph node investigations performed in accordance with the clinical protocol adopted by the authors' institution. Patients presenting with recently diagnosed breast cancer and having clinically lymph node-negative lesions under 5 cm in diameter (i.e. T1/T2N0) were invited to participate in a clinical trial approved by the local hospital ethics committee, with prior informed consent obtained from each subject.

Between 10 and 15 MBq of  $^{99m}\text{Tc}$ -labelled colloidal albumin tracer was administered. Either Albures or Nanocolloid (both Nycomed Amersham) was used for all subjects, injected in a total volume of 0.2 ml. The injection was delivered as a single bolus into the subdermal layer directly overlying the breast tumour, followed immediately by gentle massage to the injection site for approximately 1 min, performed by the patient. This was incorporated into the protocol as it has been observed to promote dissemination of the tracer, and thereby more rapid lymphatic drainage from the injection site.

Employing the aforementioned technique, a relatively small volume of tracer is administered via a single injection superficial to the lesion. This contrasts with the technique employed by some other groups, whereby colloid is typically administered via four injections into the parenchymal breast tissue.

Immediately after injection of tracer, dynamic image data were acquired for 45 min in the anterior oblique projection (256×256 W matrix; 10 s/frame for 15 min, 60 s/frame for 30 min), followed by static images collected in the anterior oblique and lateral projections (256×256 W matrix, each 5 min duration) at 1 h post-injection (p.i.). Further static data were collected at 16–24 h p.i. for all patients studied in the initial phases of the study, and for subsequent patients only if all earlier data had failed to demonstrate lymphatic drainage of the tracer to one or more sentinel lymph nodes. Late image data from these initial patients are used here. An IGE 400XC/T or 400 AC/T (General Electric Medical Systems) digital gamma camera system with a low-energy, high-resolution collimator (LEHR) was used for the acquisition of all image data, and an IGE Star computer used for data analysis.

Early dynamic image data were analysed by region of interest and time-activity curve analysis to determine the extent of the clearance of tracer from the injection site. Image data obtained at all time points in the anterior oblique projection were examined

critically for the presence of any vascular background activity of tracer, and particularly for any evidence of specific tracer uptake in the liver, spleen or bone marrow of the ribs and sternum. The thyroid was also examined for the presence of any activity, where this arises from the unbound  $^{99m}\text{Tc}$  radiolabel in the form of  $^{99m}\text{Tc}$  pertechnetate.

An estimate was made of the initial volume of dispersion of the tracer at the injection site. This was obtained by estimating the distribution of tracer in the image plane via region of interest analysis of the early dynamic image data and static data acquired at 1 h p.i. Data were obtained for 12 patients. Two patterns of distribution of tracer with depth were then modelled to obtain estimates of the volume of dispersion: in the first pattern, the tracer was considered to be constrained to an arbitrary thin but representative subdermal layer of 4 mm thickness, while in the second it was considered to be distributed throughout an arbitrary hemispherical volume whose depth mirrors the radius of its dimensions in the image plane.

Blood samples were obtained from the patients (a total of 18 samples from 14 subjects) at 1–48 h p.i.; they were primarily withdrawn between 1 and 2 h or between 24 and 48 h p.i. From each sample, 2 ml whole blood was extracted and assayed in a gamma well counter. This had been previously calibrated by counting a wide range of samples containing accurately determined activities of  $^{99m}\text{Tc}$ , thereby allowing a sensitivity factor for  $^{99m}\text{Tc}$  in cps/MBq to be directly determined for the well counter. Thus, from the whole-blood samples obtained, the % injected dose/ml whole blood was calculated, this being corrected for background activity and decay corrected to the time of injection of the tracer. This activity determination was then referenced to a standardised injected activity of 15 MBq and a reference total blood volume of 5000 ml, where this approximates to the normal total blood volume of 60–80 ml/kg for the adult female [15].

Surgery was performed at 18–24 h p.i., and the sentinel lymph node was localised prior to excising both the primary tumour and the axillary lymph node chain. Localisation of the sentinel node(s) was achieved by the use of a gamma detecting probe (Neoprobe 1500, Neoprobe Corp. Columbus, Ohio, USA) and the intra-operative administration of a vital blue dye (Patent Blue V, Laboratoire Guerbet, Aulnay-sous-Bois, France). The activity content of the sentinel lymph node(s) identified at operation was determined by gamma well counting. This was performed immediately following excision of the nodes and prior to their histological examination. The radioactive content of the node was directly determined by using the  $^{99m}\text{Tc}$  sensitivity factor for the well counter. From these data the % injected dose was also calculated, where this too was referenced to the time of injection of tracer and to a standardised tracer activity of 15 MBq. A total of 30 nodes were taken from 22 patients, and these comprised both sentinel and second-echelon nodes. Of these 30 excised nodes, the last 16 were additionally weighed to determine the typical weight range for an axillary sentinel lymph node.

*Dosimetric calculations.* The above data were used to perform a dosimetry estimate for the radiation dose arising from the subdermal administration of  $^{99m}\text{Tc}$ -labelled tracer. The biodistribution data obtained are detailed in full in the Results section; however, from these data those observations used to generate the following dosimetric estimates are summarised by the overall statement that, of the activity administered directly into breast tissue, 100% remains as a localised activity source within this tissue with negligible biological clearance of radioactivity either as colloiddally bound tracer or as free  $^{99m}\text{Tc}$  pertechnetate.

Dosimetric estimates were made for both individual organ doses and for the whole-body absorbed radiation dose. These were both based upon established MIRD methodology [16], and many of the dose calculations were performed using the MIRDOSE 3.1 dosimetry software package developed at Oak Ridge (Oak Ridge Institute for Science and Education, TN, USA – <http://www.ornl.gov/ehsd/mirdose>) [17]. The MIRD adult, non-pregnant female reference model was used to determine all dosimetric indices for this study. This model is assigned a total body weight of 58 kg, with breast tissue totalling 407 g including its overlying layer of skin.

The radiation dose to the breast itself was estimated by considering two different models. The first estimate assesses the mean radiation dose to the entire breast receiving the injection. With the modifications detailed below, this was determined using the MIRD dosimetry model for the mean dose to an organ where an idealised homogeneous tracer distribution is assumed throughout the total organ volume.

The second estimate assesses the maximum dose received only by that specific volume of the tissue which retains the total administered activity of colloidal tracer after some modest initial dissemination, where this volume is as determined from the two estimates made concerning possible patterns for this tracer dissemination into surrounding tissue. It is known that the mean range for  $^{99m}\text{Tc}$  gamma rays in soft tissue is around 46 mm [18], and as this is of the order of the dimensions of the organ it can reasonably be argued that all breast tissue other than that retaining the tracer at the injection site will receive an approximately uniform radiation dose as a result of its irradiation from this source of activity.

An estimate of the mean radiation dose to the total breast resulting from the injection of colloid based upon the MIRD methodology for individual organ doses will assume that the tracer is distributed homogeneously throughout the entire organ. In this instance this is defined as the total mass of breast tissue. An estimate of the mean dose to the breast which receives the injection of colloid will reflect the actual situation more accurately when the calculated dose is modified to account for the distribution of tracer within one breast only, and the modification applied here amounts to a simple multiplication of the MIRD-derived dose by a factor of 2. A quantitative defence of this simplistic dose-scaling approach is detailed in the Discussion.

In assigning a residence time for the tracer within the injection site for the determination of all dose estimates it has been assumed that the mass of breast tissue retaining the radioactive tracer is not excised at operation but is allowed to remain in situ. The administered activity must therefore be integrated to infinity to determine a figure for the cumulated activity within the source organ, and whilst this represents a conservative assessment of the likely situation, the model is sufficiently realistic to be preferable as a “worst-case” estimate for dosimetric purposes.

The radiation dose received by those organs immediately neighbouring the breast and the absorbed radiation dose to the whole body were also calculated using standard MIRD methodology. For these dose determinations the “unscaled” (MIRD) mean breast dose was used.

The indices of “effective dose equivalent” (EDE) [19] and “effective dose” (ED) [20] were also determined, where these have been proposed by the International Commission on Radiological Protection (ICRP) as measures of the absorbed dose “weighted” to take into consideration the relative radiosensitivity of differing tissues of the body. The “unscaled” (MIRD) mean breast dose was also used here.

### *Radiation dose to staff groups*

**Surgical staff.** The radiation dose to surgical staff was determined by issuing personal radiation dosimeters to the two surgeons performing the surgical procedure – one surgeon conducted the probe-guided localisation and excision of the sentinel node(s) and another excision of the primary tumour and axillary lymph node basin. A “bleeper” type Geiger-Müller whole-body dosimeter (Gothic Crellon Ltd., Wokingham, Berks., UK) was worn by each surgeon at the xiphisternum, underneath the outer sterile gown. Additionally, extremity dosimeters were worn by each surgeon on the index finger of the dominant hand, being placed underneath the sterile surgical glove. These consist of a small (10 mm) lithium fluoride (LiF) disc held within a latex finger-glove at the pulp of the fingertip. LiF exhibits thermoluminescence, which renders the accrued radiation dose retrospectively detectable. Both forms of dosimeter were worn by each of the two surgeons for 19 surgical procedures.

**Pathology staff.** The radiation dose to staff in the pathology laboratory was assessed by examining pathology work tasks and their scheduling, coupled with biodistribution information obtained from this study regarding the maximum activity content of the primary tumour specimen and the sentinel node itself. It is the practice of the histopathology laboratory at the authors' institution that surgical specimens are placed in fixing solution for between 18 and 36 h prior to their definitive pathological analysis, and a minimum sample preparation time of 24 h is typical in British pathology departments. A representative histopathology sample processing protocol could comprise immersion in formalin fixing solution with later definitive sectioning and staining of both the primary and the sentinel lymph node specimens by a pathology technician (estimated maximum total duration, 60 min). During this period, close contact between specimens and the pathologist's hands is estimated to occupy a maximum of 15 min for the primary specimen and 5 min for the sentinel lymph node specimens. Viewing of the prepared slices under the microscope typically occupies each pathologist for 15 min, for multiple prepared sections.

However, two further practices merit specific examination in respect of the higher radiation dose resulting to pathology staff. The first is the intra-operative analysis of the sentinel node(s), be it through techniques based on obtaining frozen sections [21] or touch imprint cytology [22], with the resulting potential for a higher level of exposure from the sentinel node(s). If performed, frozen section analysis of the sentinel node(s) may require a maximum of 45 min processing time for analysis of multiple sections. The second is the definitive examination of both the primary tumour specimen and sentinel nodes during the immediate postoperative period, as is the policy at some centres.

### *Radioactive clinical waste*

Radioactive waste created within the nuclear medicine clinic will be subject to a programme of radiation monitoring with appropriate storage until physical decay of its constituent radionuclides reduces the content to levels below relevant disposal limits. However, waste generated external to such well-controlled environments is not normally subject to routine radiation monitoring and as such its handling may not be appropriate to the radioactivity contained within.

Radioactive waste created in the operating theatre was examined by monitoring the waste material for the presence of radioac-

tivity using a suitable calibrated scintillation contamination monitor. This demonstrated an uptake of measurable levels of radioactivity confined to the surgical swabs used to absorb excess blood from the surgical field. These were therefore subjected to further analysis by quantitative measurement of their radioactive content.

This was accomplished using a gamma camera, by placing the waste swabs directly onto the collimator face of the camera together with a counting tube containing a known activity of  $^{99m}\text{Tc}$ . A static image was acquired for 30 min when the ambient radiation level was low, outside working hours. Region of interest analysis of these image data for both the swabs and counting tube then yielded a decay-corrected activity estimate for the swabs. Further studies indicated that this technique has sufficient sensitivity to permit the detection of around 2 kBq against background activity levels, where this equates to approximately 0.01% injected dose referenced to the time of injection.

Waste swabs were measured for a total of 16 surgical procedures. Eleven samples were obtained from a wide local excision procedure, where the lesion and immediately adjacent tissue only was removed. The remaining five originated from patients undergoing a mastectomy when the entire tissue of the breast was removed, incorporating the injection site en bloc.

The pathology laboratory may also generate radioactive waste if biomaterials from the processed specimens are disposed of before sufficient physical decay acts to render them effectively non-radioactive. For both of these potential sources of waste generation, the minimum duration for storage required to eliminate the possibility of this occurrence was determined, using direct activity measurements and biodistribution data obtained here for the radiolabelled tracer.

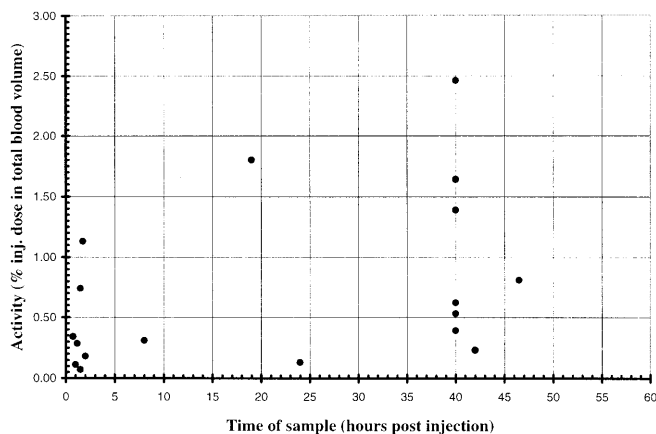
## **Results**

### *Patient dosimetry*

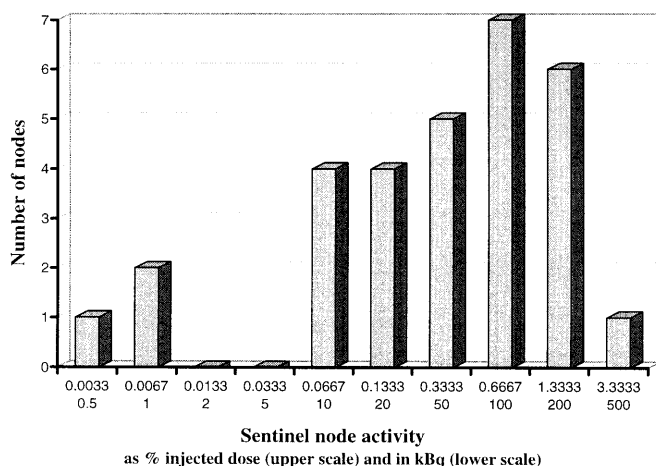
**Biodistribution data.** Analysis of the early imaging data clearly demonstrated that at least 95%, and frequently close to 99%, of the administered radioactivity is initially retained as a localised source at the injection site within the subdermal tissue layer of the breast. At later time points image data were found to indicate that a very high proportion of this tracer activity remains at the injection site for at least 24 h p.i. No evidence of uptake via the reticulo-endothelial system into the liver, spleen and bone marrow was observed from the image data obtained at any time point, for any of the patients studied. This finding was observed regardless of whether Nanocolloid or Albures was used as the radiolabelled tracer.

Data obtained from the direct assay of 18 blood samples in a gamma well counter are illustrated in Fig 1. The (decay-corrected) mean uptake of colloidal tracer was determined as  $0.73\% \pm 0.37\%$  injected dose/total blood volume (actual range 0.07%–2.46%). The maximum uptake of 2.46% was found from a sample taken at 40 h p.i., with all of the samples taken at less than 24 h p.i. returning less than 1.80% injected dose/total blood volume.

Gamma well counting of the freshly excised sentinel lymph nodes indicated that between 0.0038% and 5.14% injected dose was present within the sentinel nodes ex-



**Fig. 1.** Tracer activity present in whole blood samples taken between 1 and 48 h p.i., expressed as % injected dose present in total blood volume at the time of injection



**Fig. 2.** Sentinel node activity expressed as % injected dose and as actual activity, both referenced to the time of injection. The labelled value for each group represents the lower limit of activity for that group

amed at the time of excision (referenced to the time of injection), with a mean uptake of  $0.96\pm 1.33\%$  injected dose. Figure 2 details the results for all 30 nodes examined. For those 16 excised nodes directly measured, the weight of the node ranged from 0.29 g to 1.98 g, (mean  $0.801\pm 0.812$  g).

**Radiation dose estimates.** Applying the dose-scaling modification detailed in the previous section, the mean radiation dose to the tissue of the affected breast was determined to be  $7.20\times 10^{-1}$  mGy/MBq. This equates to a dose of 10.8 mGy for a tracer administration of 15 MBq.

The maximum, local, radiation dose received by that small volume of breast tissue retaining the tracer is somewhat higher than the dose received by the entire tissue of the breast. Image data obtained from 12 subjects demonstrated a mean lateral dispersion of tracer of

26.7 mm diameter, with good inter-subject agreement. This supports an estimate of 2–5 ml total volume of dispersion for the tracer, the exact volume depending upon whether the dispersion is assumed to occur across a thin (4 mm) subdermal layer or throughout an arbitrarily limiting hemispherical volume. When this volume range is used to generate an estimate of the local radiation dose to the tissue of the injection site itself, the resulting dose will lie between 19.9 and 44.0 mGy/MBq.

Established MIRD methodology was used to determine the radiation dose to neighbouring organs. Of these the thymus gland receives the largest radiation dose,  $9.87\times 10^{-3}$  mGy/MBq, followed by the lung, which receives a dose of  $7.79\times 10^{-3}$  mGy/MBq. These calculations result in total doses of 0.15 mGy to the thymus and 0.12 mGy to the lung for an administered activity of 15 MBq. The radiation doses to the stomach, liver, pancreas and surfaces of the bone are all less than  $3\times 10^{-3}$  mGy/MBq, with the spleen, gallbladder wall, thyroid, red marrow, muscle and adrenal glands all receiving less than  $2\times 10^{-3}$  mGy/MBq. The dose received by the remaining, more distant organs is at least 4 times lower than this lower figure, with the uterus receiving  $1.20\times 10^{-4}$  mGy/MBq and the ovaries  $1.10\times 10^{-4}$  mGy/MBq.

However, if the left breast is investigated then a measurable radiation dose will additionally result to the myocardium. This approximates to  $2\times 10^{-2}$  mGy/MBq, or 0.32 mGy per 15 MBq administration. Conversely, if the right breast is investigated, the resulting radiation dose to the myocardium is reduced by a factor of approximately 10 with respect to an injection of tracer to the left breast, based on the use of assumed values for the difference in source→target separation distances between these tissues and the myocardium.

The sentinel lymph node itself will receive a radiation dose of between 0.440 and 2.53 mGy/MBq tracer administration if a weight range is assigned spanning that determined by direct measurement and a 1.0% uptake of tracer is assumed, retained permanently from the time of injection.

The absorbed radiation dose to the total body is  $4.12\times 10^{-3}$  mGy/MBq, leading to a dose of 0.062 mGy for a 15 MBq tracer administration.

The EDE is estimated as  $5.70\times 10^{-2}$  mSv/MBq, and the ED as  $2.11\times 10^{-2}$  Sv/MBq, resulting in an EDE of 0.86 mSv and an ED of 0.32 mSv for a 15 MBq administration of tracer.

#### Radiation dose to staff groups

**Surgical staff.** The whole-body dosimeters used display the integrated dose to which they are exposed in  $\mu$ Sv ( $1\times 10^{-6}$  Sievert), in integer units and with a minimum reading of 1  $\mu$ Sv. The recorded dose is thus displayed in incrementally increasing integer units. With the excep-

**Table 1.** Occupational radiation doses to pathology staff resulting from processing and analysis of surgical samples when surgery is scheduled at 24 h post injection, assuming that the primary specimen retains 100% of a 15 MBq administered dose and the sentinel lymph node contains 5% of the administered dose. The percentage

quoted for each datum represents the estimated dose as a percentage of the relevant maximum annual dose limit: 1 mSv whole-body dose limit to a member of the public, 500 mSv finger dose limit to a radiation worker or 150 mSv dose limit to the lens of the eye for a radiation worker

Work task	Radiation dose estimated	Specimen	Dose			% Dose limit		
			At surgery	After 18 h	After 36 h	At surgery	After 18 h	After 36 h
Activity of specimen	Radioactive content at time of procedure	Primary	0.938 MBq	117 kBq	14.6 kBq	–	–	–
	Radioactive content at time of procedure	SLN	46.9 kBq	5.86 kBq	0.732 kBq	–	–	–
Immediate pathological analysis	Whole-body dose: 45 min @ 30 cm	Primary	127 nSv	Not applicable	Not applicable	$1.27 \times 10^{-2}$	–	–
	Whole-body dose: 45 min @ 30 cm	SLN	6.33 nSv	Not applicable	Not applicable	$6.33 \times 10^{-4}$	–	–
Processing	Whole-body dose: 60 min @ 30 cm	Primary	169 nSv	21.1 nSv	2.64 nSv	$1.69 \times 10^{-2}$	$2.11 \times 10^{-3}$	$2.64 \times 10^{-4}$
	Whole-body dose: 60 min @ 30 cm	SLN	8.44 nSv	1.05 nSv	0.132 nSv	$8.44 \times 10^{-4}$	$1.05 \times 10^{-4}$	$1.32 \times 10^{-5}$
Close contact with specimen	Finger dose: 15 min @ 1 cm	Primary	39.8 $\mu$ Sv	4.98 $\mu$ Sv	0.623 $\mu$ Sv	$7.97 \times 10^{-3}$	$9.96 \times 10^{-4}$	$1.25 \times 10^{-4}$
	Finger dose: 5 min @ 1 cm	SLN	664 nSv	83.0 nSv	10.4 nSv	$1.33 \times 10^{-4}$	$1.66 \times 10^{-5}$	$2.08 \times 10^{-6}$
Microscope viewing of processed slides	Dose to lens of eye: 15 min @ 30 cm	Primary	42.2 nSv	5.27 nSv	0.659 nSv	$2.81 \times 10^{-5}$	$3.52 \times 10^{-6}$	$4.39 \times 10^{-7}$
	Dose to lens of eye: 15 min @ 30 cm	SLN	2.11 nSv	0.264 nSv	0.033 nSv	$1.41 \times 10^{-6}$	$1.76 \times 10^{-7}$	$2.20 \times 10^{-8}$

SLN, Sentinel lymph node

tion of the one patient sent to surgery 4 h after injection of the tracer (injected dose 15 MBq) and attended by one surgeon only, the whole-body dose recorded by each of the two surgeons was in all cases less than 2  $\mu$ Sv per procedure, and in 20/38 cases less than 1  $\mu$ Sv per procedure. The radiation dose resulting to the one surgeon who conducted the operation scheduled at 4 h p.i. was 4  $\mu$ Sv. The mean value of the doses recorded by the surgeon performing the sentinel node biopsy was 0.21 ( $\pm$ 0.37)  $\mu$ Sv, while it was 0.47 ( $\pm$ 0.96)  $\mu$ Sv for the surgeon performing the tumour excision (by mastectomy or wide local excision) and axillary node dissection. The mean value of all readings was 0.34 ( $\pm$ 0.73)  $\mu$ Sv.

The TLD extremity dosimeter has a threshold for reliable detection of around 0.01 mSv, with a quoted resolution of 0.01 mSv (personal communication). The mean recorded finger dose was 0.06 ( $\pm$ 0.04) mSv for the surgeon performing the sentinel node biopsy and 0.12 ( $\pm$ 0.23) mSv for the surgeon performing the tumour excision, with a mean dose for all readings of 0.09 mSv. The finger dose resulting from the operation performed

at 4 h p.i. was not, at 0.07 mSv, significantly higher than the other readings obtained.

*Pathology staff.* Analysis of the primary tumour specimen and excised sentinel lymph node(s) follows local practice, with no single protocol universally adopted. Analysis and processing may be performed either immediately upon excision or subsequent to the storage period required for specific specimen preparation protocols. If a mastectomy has been performed then the primary specimen will contain the entire tissue mass comprising the injection site, and from biodistribution data obtained here it should be assumed that this may contain effectively 100% of the administered activity. The excised specimen obtained from a wide local excision procedure may also contain the injection site; alternatively its resection margins may cut through this segment of tissue and will therefore still contain a significant portion of the administered activity. The latter practice is also directly responsible for the creation of radioactive waste and is discussed further below. It is demonstrated in this study

**Table 2.** Occupational radiation doses to pathology staff resulting from processing and analysis of surgical samples when surgery is scheduled at 4 h post injection, assuming that the primary specimen retains 100% of a 15 MBq administered dose and the sentinel lymph node contains 5% of the administered dose. Percentage

quoted for each datum represents the estimated dose as a percentage of the relevant maximum annual dose limit: 1 mSv whole-body dose limit to a member of the public, 500 mSv finger dose limit to a radiation worker or 150 mSv dose limit to the lens of the eye for a radiation worker

Work task	Radiation dose estimated	Specimen	Dose			% Dose limit		
			At surgery	After 18 h	After 36 h	At surgery	After 18 h	After 36 h
Activity of specimen	Radioactive content at time of procedure	Primary	9.45 MBq	1.18 MBq	148 kBq	–	–	–
	Radioactive content at time of procedure	SLN	472 kBq	59.1 kBq	7.38 kBq	–	–	–
Immediate pathological analysis	Whole-body dose: 45 min @ 30 cm	Primary	1.28 $\mu$ Sv	Not applicable	Not applicable	$1.28 \times 10^{-1}$	–	–
	Whole-body dose: 45 min @ 30 cm	SLN	63.8 nSv	Not applicable	Not applicable	$6.38 \times 10^{-3}$	–	–
Processing of specimen	Whole-body dose: 60 min @ 30 cm	Primary	1.70 $\mu$ Sv	213 nSv	26.6 nSv	$1.70 \times 10^{-1}$	$2.13 \times 10^{-2}$	$2.66 \times 10^{-3}$
	Whole-body dose: 60 min @ 30 cm	SLN	85.0 nSv	10.6 nSv	1.33 nSv	$8.50 \times 10^{-3}$	$1.06 \times 10^{-3}$	$1.33 \times 10^{-4}$
Close contact with specimen	Finger dose: 15 min @ 1 cm	Primary	402 $\mu$ Sv	50.2 $\mu$ Sv	6.27 $\mu$ Sv	$8.03 \times 10^{-2}$	$1.00 \times 10^{-2}$	$1.25 \times 10^{-3}$
	Finger dose: 5 min @ 1 cm	SLN	6.69 $\mu$ Sv	0.837 $\mu$ Sv	0.105 $\mu$ Sv	$1.34 \times 10^{-3}$	$1.67 \times 10^{-4}$	$2.09 \times 10^{-5}$
Microscope viewing of processed slides	Dose to lens of eye: 15 min @ 30 cm	Primary	425 nSv	53.2 nSv	6.64 nSv	$2.83 \times 10^{-4}$	$3.54 \times 10^{-5}$	$4.43 \times 10^{-6}$
	Dose to lens of eye: 15 min @ 30 cm	SLN	21.3 nSv	2.66 nSv	0.332 nSv	$1.42 \times 10^{-5}$	$1.77 \times 10^{-6}$	$2.21 \times 10^{-7}$

SLN, Sentinel lymph node

that the sentinel node contains a maximum of 5.14% of the administered activity, and so a figure of 5% uptake has been used to derive “worst-case” estimates for the radiation dose resulting from exposure to the sentinel lymph node specimen.

Results for an estimation of pathology staff doses are presented in Tables 1 and 2 for a number of specific work tasks. Doses are estimated resulting from surgery performed at both 24 h and 4 h after administration of tracer, and for exposure to both the primary specimen and the sentinel lymph node. For both surgical schedules, specimen processing and analysis tasks performed in the pathology laboratory are estimated when performed (a) immediately after surgery, (b) after 18 h immersion in fixing solution subsequent to excision and (c) after a total of 36 h such storage following excision.

The whole-body dose resulting from analysis of both specimens immediately after surgery, as may be adopted for frozen section analysis or imprint cytology, is estimated for 45 min total exposure time at a mean mid-body to specimen distance of 30 cm. The whole-body

dose received from a definitive analysis of both specimens is estimated for a total of 60 min exposure at the same distance – where this will probably only be fulfilled for the sentinel lymph node if multiple sections are prepared. The maximum radiation dose to the fingers will be higher than the whole-body dose, and is more dependent upon the exact processing procedure performed. An average separation distance of 1 cm from the fingers to active specimen has been assumed; as actual contact with the bulk primary specimen at this distance is unlikely to exceed 15 min, this duration of contact has been used in estimating the finger dose, with 5 min assumed for contact with the sentinel lymph node. The radiation dose to the eye resulting from exposure due to viewing the processed slides is also considered here. A maximum of 15 min exposure at 30 cm eye to specimen distance has been assumed for both specimens, where, again, this will probably only be met in practice for the sentinel lymph node specimens if serial sections are analysed and viewed. The specific dose-rate constant for an unattenuated  $^{99m}\text{Tc}$  source in air was taken to be 0.18  $\mu\text{Sv}/\text{MBq}$

per hour and 0.17 mSv/MBq per hour, at 30 cm distance and 1 cm distance respectively [23].

For the data presented, all dose values presented in Tables 1 and 2 may be linearly re-scaled for exposure times differing from that quoted, and correspondingly for different administered tracer activities and the analysis of multiple sentinel lymph node specimens. The inverse-square law for radiation exposure may also be applied to estimate the dose rate resulting from exposure to sources at different distances from those quoted here, where this relationship can be defined by considering that the dose rate is proportional to the inverse of the source-subject separation distance raised to the second power.

In processing and handling radioactive specimens there is also the potential for contaminating equipment, and the use of contamination monitors is advised to assess the level of activity adhering to items of equipment which are likely to become contaminated, e.g. microtome. If positively identified, such contamination may then be removed without undue difficulty. However, cleaning materials, e.g. wipes, may then require to be stored and disposed of as radioactive waste.

#### *Radioactive clinical waste*

Waste sterile swabs resulting from 16 surgical procedures were measured for their radioactive content, and the result referenced to the % injected dose (ID) at the time of injection (for 15 MBq administered activity). The mean activity content for all 16 samples was 4.89% ( $\pm 6.14\%$ ) ID, but a clear distinction between the activity content of those swabs used during wide local excision and mastectomy procedures was evident. The mean activity content for the 11 swab samples used during a wide local excision was 7.10% ( $\pm 6.39\%$ ) ID, compared with 0.03% ( $\pm 0.08\%$ ) ID for those used during a mastectomy ( $P=0.004$ ). The most active sample from a wide local excision contained 21.89% ID, with six other samples containing between 5% and 10% ID. This maximum recorded figure corresponds to an activity content of 205 kBq at 24 h p.i.

Waste may also be created in the pathology laboratory if waste biomaterials discarded from the bulk specimens are disposed of without further storage. Decontamination of equipment may also lead to the production of waste from cleaning materials. At 4 h p.i. the primary specimen may contain up to 9.4 MBq tracer, and the sentinel node(s) a maximum of 0.47 MBq. At 24 h p.i. these values fall to 0.94 MBq and 47 kBq respectively, and after a further 48 h delay for fixing the specimens they will be only 4 kBq and 0.18 kBq.

## Discussion

### *Patient dosimetry*

It is clear from the biodistribution data obtained that a subdermal injection technique results in an absence of any visually discernible migration of the colloidal tracer via the lymphatic system beyond the sentinel node, which receives a mean uptake of only 0.96% of the injected dose, or the second-echelon lymph nodes whenever these receive tracer through spillover from the sentinel node. Specifically, no visual evidence of any uptake via the reticulo-endothelial system into the liver, spleen and bone marrow is observed. The concentration of tracer in circulating blood samples is very low, with a maximum of 2.46% found in the total blood volume at 40 h p.i. Uptake of tracer into the sentinel node itself is also low, ranging from an extremely low figure of 0.0038% to just over 5% for one sample only, with a mean uptake of just under 1% injected dose. Taken together, these findings confirm that the tracer is almost entirely retained within interstitial tissue spaces at the injection site and that only a small fraction of the tracer migrates, effectively exclusively, via the lymphatic system to the sentinel lymph node, reaching further, to second-echelon nodes, only in a small proportion of cases.

These findings are observed regardless of whether Nanocolloid or Albures is used as the colloidal tracer. It has been stated for Nanocolloid that 95% of the colloidal particles have a diameter less than 80 nm [24], and for Albures that 90% of particles have a diameter in the range 200–1000 nm [24, 25], with a mean diameter of 500 nm [26]. Although spillover of tracer into second-echelon nodes has been noted for Nanocolloid [24], it is regarded as minimal. It would seem from the observations obtained here that the variation in particle size represented by their different size range does not lead to a noticeable difference in the overall biodistribution of the two tracers.

The estimated mean breast radiation dose of 10.8 mGy for a tracer administration of 15 MBq is relatively low when compared with the range of radiation doses resulting from typical nuclear medicine procedures. The adult non-pregnant female reference model devised by MIRD and used for the derivation of this estimate for mean breast dose has an assigned total body weight of 58 kg, with breast tissue totalling 407 g (including an overlying layer of skin). The rather low figure represented by this MIRD model will lead to a human subject with breast tissue totalling in excess of this figure receiving an even lower mean radiation dose to the breast; conversely, tissue constituting a smaller breast will receive a correspondingly larger mean breast dose.

Whilst the dose-scaling approach adopted by this study to determine the mean dose to the total breast may be regarded as relatively simplistic, it can be shown to be valid if the relative magnitude of the doses due to cross-

irradiation and self-irradiation is considered – where these doses depend upon their respective MIRD S-factors (geometrical weighting factors determining the radiation dose to a “target” organ from a “source” organ which concentrates radioactivity). The dose due to cross-irradiation is defined here as the dose received by the tissue of the contralateral breast due to radiation arising from the tracer activity within the tracer-containing breast, and the dose arising due to self-irradiation is defined as the dose received specifically by the tissue of the tracer-containing breast due to local irradiation by the administered tracer. By assessing the S-factors derived for  $^{99m}\text{Tc}$  for analogous MIRD source organ→target organ cross-dose and source organ→source organ self-dose geometries, the relevant dose weighting factor for the component due to self-dose from the affected breast can be seen to be at least an order of magnitude higher than the dose received by the contralateral breast due to cross-irradiation, and often significantly more. As an example, examination of the MIRD adult male reference model for  $^{99m}\text{Tc}$  yields a spleen→spleen self-dose of  $2.33 \times 10^{-5}$  mGy/MBq for a spleen weighing 183 g compared with a spleen→myocardium cross-dose of  $1.67 \times 10^{-7}$  mGy/MBq for myocardial tissue totalling 316 g – the self-dose here exceeding the cross-dose by a factor of more than 100. Thus, the effect of this latter component upon the mean organ dose (to both breasts) is negligible and for the purposes of this estimate can be safely ignored. Furthermore, data obtained using MIRDOSE 3.1 software indicate that the radiation dose due to self-irradiation by a homogeneous distribution of activity within an idealised 200-g spherical tissue mass differs by less than 5% from the scaled mean organ dose determined by the above method, where this mass represents approximately half the total mass of breast tissue incorporated in the MIRD adult, non-pregnant female reference model. This would seem to confirm that the effect due to cross-dose is negligible.

On the basis of the above calculations, the mean radiation dose to the normal tissue of the contralateral breast will be at least an order of magnitude lower than the dose received by the breast into which the tracer has been injected – i.e. less than  $7.2 \times 10^{-2}$  mGy/MBq or 1.1 mGy for an administration of 15 MBq.

Standard MIRD methodology does, however, assume that tracer activity is homogeneously distributed throughout the tissue of the organ under investigation. As discussed, this is not a true model for the sentinel node technique, where the tracer administration technique used will result in a subdermal bolus of tracer after the 0.1 ml total volume of tracer solution has been injected and disseminated by the recommended massage procedure. This volume of retention of tracer has been estimated from scintigraphic data to be approximately 2–5 ml, and so the radiation dose received by that small volume of breast tissue retaining the tracer will be appreciably higher than that received by the remaining tissue

of the breast. Using this figure for the estimated retention volume of tracer the maximum local radiation dose to breast tissue at the injection site is estimated as ranging between 20 and 44 mGy/MBq. This equates to a 0.30 to 0.66 Gy dose for 15 MBq administration of tracer, and is thus approximately 30- to 60-fold higher than the estimated mean radiation dose to the breast as a whole. These data are in good agreement with the findings of Bronskill [27], who determined the radiation dose to local tissue resulting from internal mammary lymphoscintigraphy performed by the interstitial injection of  $^{99m}\text{Tc}$  antimony sulphur colloid. He calculated this to be a mean of 45.6 rads (equivalent to 0.456 Gy) from the application of MIRD methodology to scintigraphic observations of the nodal uptake of tracer and its subsequent kinetics.

The maximum radiation dose to the breast local to the injection site will obviously be dependent upon the exact volume of tracer dispersion, and when this alters, for example when a different injection technique is adopted, then the resulting dose will differ. Thus these data are not directly applicable to sentinel node studies performed using an alternative administration technique. The multiple administrations associated with a peritumoral injection technique will tend to increase the total volume of dispersion of tracer and so will act to reduce the radiation dose per MBq total administered activity, though the significance of this difference is likely to be minimal.

In assessing the radiation dose, and hence the risk, resulting to the patient, both the mean dose to the breast and the maximum radiation dose received by breast tissue at the site of injection should be considered in relation to the residence time of the administered activity within the breast. The sentinel lymph node and the primary tumour will be excised at operation, where this is typically scheduled to take place between 4 and 24 h after the tracer is injected. The excised primary tumour specimen may also include that peritumoral tissue or subdermal tissue overlying the tumour which comprises the injection site (as when a mastectomy is performed), and this will therefore contain effectively all of the administered activity. However, some of the colloid-bearing tissue may be left in situ if a less radical surgical procedure is adopted, such as a wide local excision, and thus the magnitude of the radiation dose resulting to the patient will depend upon the specific surgical procedure followed. Complete removal of the colloid-bearing tissue at operation is more typical and this acts to reduce the radiation dose, although it should be emphasised that the effect has minimal impact upon the overall dose resulting from the administration of tracer: at 24 h p.i. the  $^{99m}\text{Tc}$  radiolabel will already have undergone significant radioactive decay consistent with the passage of four physical half-lives ( $^{99m}\text{Tc}$   $t_{1/2} = 6.02$  h) such that it retains only 1/16th (6.25%) of its initial radioactivity. This will lead to a relatively minor increase in the resulting radiation dose if the tissue is not excised but remains in situ.

With regard to the radiation dose received by the affected breast it should also be noted that this may be subject to a postoperative course of external beam radiotherapy, where a 50 Gy radiation dose is typically prescribed in this context [28]. However, this does not invalidate the need to determine the radiation dose received from the sentinel node procedure alone, and more importantly, the nature of the resulting dose distribution.

The radiation dose to all other organs can be seen to lie approximately two orders of magnitude below the mean dose estimated to result to the breast, and at around 0.1 mGy for a 15 MBq administration of tracer it is effectively negligible when assessing the radiation risk to the patient. The radiation dose received by the sentinel lymph node itself is estimated as being between 6.6 and 38 mGy for 15 MBq administration of tracer. Having a similar volume to the dispersion volume of tracer, and with the range of tracer uptakes reported above, the sentinel lymph node receives a radiation dose significantly lower than that received by the breast tissue local to the injection site, and it will moreover be excised from the body to enable the sentinel node biopsy to be performed.

At 0.06 mGy for a 15 MBq administration the estimated whole-body absorbed radiation dose is low relative to many typical nuclear medicine investigations, but the extreme heterogeneity of the tracer's biodistribution here reduces the relevance of this index with respect to its role in assessing the level of risk resulting from more uniformly distributed, systemically administered agents.

Two indices for internal radiation dosimetry have been developed by the International Commission on Radiological Protection (ICRP) to attempt to assess the level of risk arising from exposure to radiation. The concept of the "effective dose equivalent" (EDE) was defined in 1977 [19] as the sum of calculated dose equivalents determined for a set of specified bodily organs, where each contributing organ dose was multiplied by a weighting factor  $w$  to obtain the dose equivalent accounting for the relative radiosensitivity of that organ. The EDE was thus a "weighted" total whole-body radiation absorbed dose. "Effective dose" (ED) was introduced by the ICRP in 1990 [20] to supersede the EDE. Although the ED was developed from similar underlying concepts, it incorporates revised tissue weighting factors  $w_T$ , determined for an expanded set of body organs, where these organs are derived from a reference population comprising an equal number of males and females covering a wide age range. The ED thus has the advantage that it better reflects the total risk to the whole population in addition to that to radiation workers, and is therefore more applicable for use in assessing both medical and public, in addition to occupational, radiation exposures. Acceptance of the ED as a replacement for the EDE has not been universal, however, and both quantities are still in use for dosimetric purposes. In practice, the radiation dose resulting from different radiopharmaceutical administrations may

be compared using either quantity – both in comparing the dose resulting from each investigation and in relating this to the dose resulting from an "equivalent" exposure caused by uniform irradiation of the whole body. Neither the ED nor the EDE is fully endorsed by the nuclear medicine community [29], however, and use of the equivalent radiation dose to individual organs only is still advocated by some authorities.

The EDE resulting from a sentinel node investigation is estimated here as  $5.70 \times 10^{-2}$  mSv/MBq, and the ED as  $2.11 \times 10^{-2}$  mSv/MBq. This results in an EDE of 0.86 mSv and an ED of 0.32 mSv for a 15 MBq administration of tracer. The difference in the value returned for these two indices is largely due to the very different tissue weighting factor  $w_T$  accorded to breast tissue for each of the two quantities, i.e. 0.15 for the EDE [19] and 0.05 for the ED [20]. To effect a comparison of these results, data published by other workers in respect of conventional lymphoscintigraphy were reviewed. Bergqvist et al. [30] reported an EDE of  $5.32 \times 10^{-3}$  mSv/MBq for lymphoscintigraphic studies performed to investigate malignant melanoma via the subcutaneous injection of  $^{99m}\text{Tc}$  antimony sulphur colloid. An EDE of  $1.25 \times 10^{-2}$  mSv/MBq [31] has been quoted for general diagnostic lymphoscintigraphy procedures for licensing purposes in the United Kingdom, and has recently been superseded by a figure of  $1.00 \times 10^{-2}$  mSv/MBq quoted for the ED [32]. However, it must be noted that for all of these applications the technique adopted differs from that for the sentinel lymph node investigation detailed here. Certainly the relatively high radiosensitivity of breast tissue and its raised tissue weighting factor will elevate the resulting ED or EDE with respect to an otherwise identical tracer administration in a location accorded a more typical tissue weighting factor. This situation would be encountered, for example, when the tracer is injected into a limb, as is frequently the case for malignant melanoma. It is pertinent to consider the merits of a tissue weighting factor  $w_T$  for the breast modified to better reflect the risk (or more specifically the detriment) to this almost exclusively female cohort of patients (with its associated and specifically biased age distribution), as the weighting factor results directly from known data regarding the detriment for a *specified* population. However, further consideration of this issue is unfortunately beyond the scope of this study.

Since the ED has been proposed by the ICRP as being more appropriate for the assessment of risk in the whole population, it is this index which has been used for comparative purposes in the following discussion, which places in context the radiation risk arising from a sentinel node study. When the ED estimated for the sentinel node mapping procedure in breast cancer is compared with the ED resulting from a number of commonly performed nuclear medicine and radiographic procedures (Table 3), it is clear that it lies at the lower end of a wide range of radiation doses, being approximately 16 times

**Table 3.** Effective dose for a number of commonly performed nuclear medicine and radiographic procedures (from data published by the Royal College of Radiologists [33], Perkins [34] and AR-SAC [32])

Investigation	Effective dose (mSv)
Sentinel lymph node study	0.32
<sup>99m</sup> Tc bone scan	3
<sup>99m</sup> Tc perfusion lung scan	1
<sup>123</sup> I thyroid scan	4
<sup>99m</sup> Tc scintimammography study	11
Chest X-ray	0.02
Mammography	0.4
Plain film abdominal X-ray	1.0
Lumbar spine X-ray	1.3
Intravenous urography	2.5
Barium meal	3
Brain CT	2.3
Abdominal CT	10
Chest CT	8

higher than that for a chest X-ray and similar in magnitude to the radiation dose resulting from a mammogram.

It is educative to compare the radiation dose resulting from a sentinel lymph node study more generally against the radiation dose resulting from a number of natural causes [35]. It is of comparable magnitude to that experienced from cosmic rays during a long-haul airlight (London-New York return trip: 0.06 mSv), or due to residence at high altitude (Denver, USA: 0.88 mSv/year) or in an area overlying granite bedrock and therefore susceptible to the ground release of radon (2 weeks' residence in Cornwall, UK: 0.25 mSv).

More widely, the ICRP [20] have recently asserted that an ED of 1 mSv will result in a total detriment to the individual of  $7.3 \times 10^{-5}$  (73 per million), where detriment is defined as the total risk due to the induction of all cancers, both fatal and non-fatal, and of severe hereditary effects. The risk of fatal cancer induction alone is stated as being  $5.0 \times 10^{-5}$  (50 per million). This equates to a total detriment for the 0.32 mSv ED resulting from a sentinel node procedure of 23.4 per million, equal to a probability of 1 in 42,808, and a risk of induction of fatal cancer of 16 per million, equal to a probability of 1 in 62,500. The risks resulting from a number of everyday life activities are also known, and it is pertinent to compare these against the risk of induction of a fatal cancer resulting from an exposure to 1 mSv radiation dose. This latter risk has been determined to be equal to the risk resulting from smoking 75 cigarettes, or drinking 1 glass of wine daily for 6 months, or travelling 125 miles by motorcycle, 2500 miles by automobile or 16,000 miles by aeroplane, or rock climbing for 75 min or canoeing for 5 h (data obtained from Shields and Lawson [36] and Pochin [37]).

### Radiation dose to staff groups

Within the countries of the European Community, annual radiation dose limits are required to be reduced [38] to comply with the current recommendations issued by the ICRP [20], and legislation to effect this is imminent in the United Kingdom. The annual dose limit to the whole body for a radiation worker will then fall to 20 mSv, with a 1 mSv limit for a member of the public. This latter category also applies to all members of staff other than those designated as radiation workers. Special consideration should be given to any member of staff who is pregnant as specific lower dose limits apply to all pregnant staff in respect of the radiation dose resulting to the foetus. Here the 1 mSv dose limit to a member of the public is applicable, and if required, regular monitoring of pregnant staff by the issue of a whole-body dosimeter (in the form of a "radiation badge") will help to ensure compliance with this limit. The radiation dose limit to extremities of the body for a radiation worker will remain at 500 mSv per year [38], and that to the lens of the eye at 150 mSv, where the latter figure is derived from consideration of the threshold radiation dose necessary for formation of a cataract.

In reassuring staff who are otherwise not exposed to radiation during the course of their work, it is helpful to consider the dose estimates and direct measurements quoted here in the context of the data cited in the previous two paragraphs – regarding natural sources of radiation exposure and the risk associated with everyday life activities.

The mean whole-body dose to surgical staff resulting from surgery performed on a sentinel node patient is 0.34  $\mu$ Sv, with the maximum recorded dose below 2  $\mu$ Sv. This represents a very small fraction of the dose limit to a member of the public and, based upon the mean whole-body dose, up to 3000 procedures could be performed per year before even this dose limit is exceeded. Use of the maximum recorded dose would suggest a ceiling of 500 procedures per year. This is clearly unlikely to occur in all but the busiest surgical practices. The mean finger dose of 0.09 mSv recorded here represents less than 1/5000th of the relevant dose limit, i.e. for a surgeon who has been designated as a radiation worker. Again, it is deemed unlikely that this limit will be exceeded in practice.

The radiation dose resulting to pathology staff clearly depends upon the scheduling of the procedures performed: due to radioactive decay and its effect on radioactivity present within specimens, doses resulting from surgery at 24 h p.i. are systematically approximately 10 times lower than those resulting from surgery performed at 4 h p.i. Furthermore, doses derived from analysis of sentinel lymph node(s) are at least 20 times lower than those resulting from analysis of the primary specimen at the same time point owing to the lower activity of the former.

Whole-body doses are very low, with only an analysis of the primary specimen immediately upon completion of surgery scheduled at 4 h p.i. leading to an estimated dose of a magnitude likely to impact upon occupational dose limits, at approximately 1/600th of the annual dose limit to a member of the public, or 1/12,000th of the maximum dose limit to a radiation worker. Moreover, analysis at this point is usually only ever performed upon sentinel lymph node specimens, where the equivalent dose is approximately 1/12,000th of the dose limit to a member of the public. The radiation dose to the fingers is perhaps the more relevant risk to this staff group, but 15 min close contact with the primary specimen at 4 and 24 h p.i. leads to estimated doses representing approximately 1/1250th and 1/12,500th of the dose limit to a radiation worker respectively. Moreover, the radiation dose to the lens of the eye resulting from prompt analysis of slides prepared immediately following surgery at 4 h p.i. is estimated to be less than 1/300,000th of the specified dose limit to this organ for a radiation worker.

However, these data serve to demonstrate that, if a sentinel node biopsy programme is established with a *very significant* patient workload, and if histological analysis of the primary specimen is routinely conducted *immediately after early surgery*, then estimated finger doses suggest that staff members involved may merit designation as radiation workers for this purpose, with finger doses being monitored by the use of TLD extremity dosimeters until the actual level of exposure may be more accurately determined. Whole-body dosimeters may also be worn to establish the whole-body dose. For all other situations, staff doses resulting from contact with specimens are likely to be below measurable levels, of a level too low to have an impact upon occupational dose limits.

It is relevant here to note that radiation dose estimates performed by the authors for a risk assessment prior to commencement of the study led to estimates for the total body and extremity doses to surgical staff notably in excess of the doses actually measured; this would seem to be primarily attributable to over-estimates of the time spent in direct contact with the radioactive specimens. Thus, a similar "worst-case" over-estimate of the radiation dose resulting to pathology staff may be expected to result from these dose determinations, although they may be usefully applied to estimate the radiation dose received by surgical staff under circumstances which differ from those applying to the direct measurements reported here.

When transporting specimens to the pathology laboratory they should be securely sealed within a suitable container, and should be clearly labelled as belonging to a patient who has undergone a sentinel node procedure. Staff involved in transporting these specimens both on-site and off-site should be aware of the radioactivity contained within the samples, and may be reassured that the risk resulting from transportation of the samples is negli-

gibly small. Expert radiation protection advice should be sought locally in respect of the requirements regarding transportation of radioactive materials beyond the hospital site, as in many countries such operations are subject to specific further legislation [39].

Whenever staff come into direct contact with radioactive materials there is an additional risk of radiation exposure due to the internalisation of this radiation, through its inhalation or ingestion. Annual limits for the internal intake of  $^{99m}\text{Tc}$  have been specified for both routes of internalisation [40] and far exceed the likely level of any unintentional intake resulting from such an incident. Providing standard biohazard precautions are followed, including the use of gloves and appropriate protective clothing at all times, then the risk of this form of exposure should be effectively eliminated.

#### *Radioactive clinical waste*

It has been shown from direct monitoring of the waste generated in the operating theatre that surgical swabs represent the only detectable source of radioactive waste arising from procedures for the management of breast cancer. Data obtained from measurement of their radioactive content indicate that significant levels of contamination are present in these items, and it is clear that the level of this contamination is dependent upon the exact surgical procedure performed. More specifically, this contamination would seem to be a direct consequence of the swab contacting such exposed tissue at the injection site as has retained the radiolabelled tracer in high concentration. Thus the transfer of even a minimal fraction of this activity may render the swab measurably contaminated. This would explain the high levels of contamination seen in swabs used in a wide local excision procedure, where the injection site may be exposed at the resection margins of the excised tumour, and the relatively low levels observed in swabs used in a mastectomy procedure, where tissue including the injection site is left intact within the excised specimen. This is an important finding, as it highlights the mechanisms by which significantly contaminated waste may be generated during other surgical procedures. Certainly, it seems clear that items not placed in contact with the tissue comprising the injection site are highly unlikely to become contaminated to a level detectable with monitoring equipment.

It should also be noted that radioactively contaminated swabs, by virtue of their high radioactive content, have the capability to affect intra-operative detector measurements if they are placed in close proximity to the probe while it is used to detect the relatively low level of uptake observed in sentinel nodes. Thus care should be taken to ensure that they are kept clear of the immediate vicinity of the probe while it is in use.

From a knowledge of the activity present in pathology specimens taken from the sentinel node patient it is clear

that their radioactive content may be in excess of that mandated for disposal as non-radioactive waste. Thus specific arrangements for the storage of radioactive waste prior to disposal may be required if disposal of declared radioactive waste is not permitted. Legal requirements for disposal of "dustbin-level" radioactive waste differ between countries, but as an example United Kingdom legislation [41] and its associated guidance specifies as "very low level waste" (VLLW) waste placed in sealed bags or bins that has an activity concentration below 400 kBq/0.1 m<sup>3</sup> (and below 40 kBq per article) and exempts such waste from the need for further processing, provided that it is consigned specifically to landfill [42]. However, radioactive waste requiring incineration due to the nature of its contents (e.g. clinical waste) must meet a much lower maximum activity concentration of below 400 Bq/kg for it to be regarded as "non-radioactive" and therefore suitable for disposal via this route [43]. This latter stipulation in particular is a stringent requirement, and necessitates that the primary specimen be stored for around 3 days from the time of surgery before its radioactivity concentration falls to meet this level. The routine storage of pathology specimens beyond this period may, however, be existing practice.

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