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Handling of radioactive seed localisation breast specimens in the histopathology laboratory: the Western Australian experience

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Summary

Radio-guided occult lesion localisation using iodine-125 seeds (ROLLIS) is a novel method of localisation for impalpable *in situ* and invasive carcinomas that has been the subject of a recent pilot study and pilot study extension in Western Australia. Robust protocols for radiation safety, specimen labelling, specimen tracking, seed retrieval and seed disposal were developed at two Western Australian laboratories to minimise the risk of seed loss. The processes are safe and effective with no significant radiation exposure to pathologists and with acquisition of all seeds intact and undamaged. The success can be attributed to developing specific seed retrieval techniques, suited to local preferences at each institution, with input from surgeons, radiologists and medical physics personnel. These techniques are now routine and will continue in the randomised control phase of the ROLLIS study.

Key words: Breast neoplasm, breast-conserving surgery, iodine-125, lumpectomy, radiation safety, radioactive seed localisation, RSL, specimen handling.

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INTRODUCTION

The prevalence of breast cancer is increasing, largely due to an ageing population and increased detection through national mammographic screening programs such as BreastScreen.[1] Screening results in the increased detection of impalpable *in situ* and invasive carcinomas requiring some form of localisation procedure to facilitate excision.[1] Radio-guided occult lesion localisation using iodine-125 seeds (ROLLIS), is a novel localisation technique using small 4.5 × 0.8 mm titanium seeds containing low activities (<4 MBq) of the radioisotope iodine-125 (I-125) (Fig. 1). A seed is placed into an impalpable breast lesion, or multiple seeds are inserted to 'bracket' a lesion, via an 18 G needle using ultrasound and/or stereotactic guidance by a radiologist. The subsequent excision is guided by the location of the seed(s) which are identified in theatre with a gamma probe. ROLLIS does not interfere with sentinel node procedures, since the energy of the principal photon emissions of iodine-125 is substantially different to those of the technetium-99m radioisotope (around 30 keV versus 140 keV). The radiation dose to the breast for a 2 MBq seed *in situ* for 12 h is very low and comparable with a two view mammogram. Recent studies have shown improved re-excision rates with ROLLIS compared to traditional hook-wire localisation techniques, and that ROLLIS may prove to be a more flexible, acceptable, efficient and effective method of excising occult breast lesions.[2–6]

A ROLLIS Pilot Study (RPS) and ROLLIS Pilot Extension Study (RPES) have recently been completed at QEII Medical Centre (QEII) and Royal Perth Hospital (RPH) in Western Australia as a prelude to a large randomised control trial (RCT) which is investigating clinical outcomes of ROLLIS compared to standard hook-wire localisation techniques. During the RPS and RPES we aimed to develop safe and effective procedures for the pathological handling of ROLLIS specimens to minimise risk of seed loss, radiation exposure and to incorporate these procedures into the routine pathology practice of two separate Western Australian pathology laboratories.

MATERIALS AND METHODS

New procedures were developed without using radioactive materials ('dummy run') and rehearsed using chicken breast prior to handling ROLLIS specimens.

All personnel involved in handling ROLLIS specimens received mandatory training prior to their participation. Written and oral instructions on radiation safety were given, including a demonstration of radioactive material and the use of radiation monitoring equipment. Local working rules (LWRs) were established for each discipline, covering radiation safety and the radiological, surgical and pathological aspects of the procedure. LWRs were signed by all personnel indicating they understood the rules and would abide by them. Radiation dose rates from handling I-125 seeds were calculated and typical workflow in the pathology lab observed to estimate likely exposure to personnel during the specimen journey.

Seeds were stored until required within the medical physics departments at the two hospitals. Seeds were ordered from medical physics by a nuclear medicine practitioner or a radiologist holding a license for radioisotopes by

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Fig. 1 Radioactive seed. The seed, measuring 4.5×0.8 mm, has a titanium outershell which protects a radioactive iodine-125 core.

completing a radioactive seed tracking form developed with collaborative input from all involved departments (Fig. 2). This form accompanied the seed(s) throughout its journey, providing a reference as to the number of seeds ordered, inserted and retrieved from the patient/specimen by the surgeon and pathologist for return to medical physics. Together with log-books recording seed transfer from the breast centre to pathology, and another recording transfer from pathology to medical physics, this form provided accountability for the seed(s) at any time and was ultimately archived in medical physics.

Women over the age of 40 who were not pregnant or lactating and who had a non-palpable breast lesion (benign, atypical/indeterminate or malignant on core biopsy) suitable for breast conserving surgery were eligible. Periareolar lesions were included providing isotope guided sentinel node biopsy (SNB) was not required (to avoid potential interference between periareolar injection of Tc-99m for SNB and detection of signal from I-125 seed). Women who had recent administration of a radioisotope with a long half-life that could cause interference (e.g., gallium-67 or thallium-201) were excluded.

After informed consent was obtained, each eligible participant had lesion localisation performed with both seed(s) and hook-wire(s). The purpose of the hook-wire was to provide a 'back-up' method of lesion localisation in case of any difficulty whilst the surgeons became familiar with using the seed. The surgeons used the seed(s) to guide the excision wherever possible. Whilst the presence of high counts within the specimen using the gamma probe provided immediate confirmation of seed removal, an intra-operative specimen radiograph (IOSR) was always taken to confirm the seed and lesion were within the specimen, and to highlight obvious close margins for immediate re-excision. For radiographically occult lesions, specimen ultrasound was also performed. The specimen was then placed in a container (labelled as per National Pathology Accreditation Advisory Council (NPAAC) guidelines[7]) with the addition of a radioactive hazard sticker (Fig. 3), indicating the number of seeds within (Fig. 4A, 5A). Radioactive hazard stickers were mandated by Western Australian Radiation Safety Regulations[8] as each low dose seed has a long half life (59 days) and exceeds the exempt limit for I-125. The accompanying request form (also filled out according to NPAAC guidelines[7]), required a ROLLIS participant sticker, indicating the number of seeds in the specimen. The specimen and the accompanying request form were then delivered to pathology.

In addition to standard personal protective equipment, ambient and electronic personal radiation monitoring devices were worn by some personnel during the RPS to measure the radiation exposure during seed handling. Calculations of dose rates indicated that doses would not be measurable above background and so devices were only provided to those personnel found during workflow observations to have the longest handling durations and most proximal handling distances; pathologists, surgeons and radiologists. Owing to minimal close handling, pathology technicians and other laboratory personnel did not require monitoring.

At QEII specimens were received in the 'fresh' state and handled immediately. Specimens were received pinned to a re-usable Perspex grid with imprinted radiopaque co-ordinates accompanied by a specimen radiograph and a pro-forma reporting sheet documenting the co-ordinates of the seed(s) (Fig. 4B,C). A pin was inserted at this co-ordinate (Fig. 4D) which guided a sagittal incision for seed retrieval, usually limited to a single slice through superficial aspect of the specimen. The seed was retrieved by direct visualisation aided by a scintillation counter and a gamma probe if required (Fig. 4E). The seed(s) was placed into a lead container labelled with a patient identification sticker, the date and the radioactive hazard sticker from the specimen container. The retrieval incision was re-approximated and held with pins (Fig. 4F). The specimen was re-examined with the scintillation counter to ensure the absence of a radioactive signal. The seed(s) were collected by medical physics personnel for radioactive waste storage prior to disposal. The specimen was then fixed overnight prior to routine handling the following day. Tissue sampling, targeting the lesion, was based on the pre-fixation specimen radiograph and the gross appearance of the specimen slices, hence a further post-fixation radiograph was not performed.

At RPH seed and lesion removal were confirmed as above. Specimens were received fresh, oriented and pinned on a tray. They were weighed and placed in formalin for overnight fixation. If this required transfer to another container the radioactive hazard sticker was also transferred (Fig. 5A). Following fixation, specimens were placed in light compression within a re-usable Perspex holding device with imprinted radiopaque grid co-ordinates and sent for further specimen radiography (Fig. 5B). The radiologist completed a pro-forma reporting sheet noting the co-ordinates of the lesion and seed(s) (Fig. 5C) and the specimen returned to pathology. The post-fixation specimen radiograph assisted in targeted sampling of the lesion. Pins were inserted into the specimen 'bracketing' the lesion and seed(s) (Fig. 5D). The specimens were then handled routinely with differential inking followed by serial sagittal sections. The seed(s) was retrieved from one of the slices between the pins by direct visualisation with the help of a scintillation counter, if required (Fig. 5E,F). The specimen was examined again with a scintillation counter to ensure the absence of a radioactive signal. The seed(s) was placed in an Eppendorf tube and into a lead container, labelled and dated as above, which was collected by medical physics personnel for storage and disposal.

As an additional 'safety-net' the number of pathologists permitted to handle these specimens at QEII was limited to a core group of pathologists with a specific interest in breast pathology.

A standardised protocol was developed in case of a radioactive seed being misplaced. All personnel, drapes and equipment in the procedure room were to be quarantined and medical physics contacted to perform a radiation survey using a scintillation counter to locate the seed.

RESULTS

The RPS and RPES involved ROLLIS specimens from 116 patients; 62 at QEII and 54 at RPH.

The radiation exposure to personnel from a typical 2 MBq ROLLIS specimen at a close handling distance of 30 cm for 30 min is about 0.4 μSv, well within the public dose limit of 20 μSv in any 1 h.[8,9] I-125 has a half-life of 60 days so there is no appreciable radioactive decay over the time frame of specimen handling; from the time of specimen collection from the operating theatre, point of receipt in the laboratory, during time of macroscopic handling, and seed retrieval. To reach the public limit of 1 mSv/yr (above a background of 2 mSv/yr) a person would need to sit 30 cm from an unshielded 2 MBq I-125 seed for 5 h per day, 5 days a week for 52 weeks of the year, implausible for normal handling of the seed. Radiation exposure to pathologists and surgeons was confirmed to be negligible and not measurable above background levels as assessed by the use of ambient and electronic personal radiation monitoring devices during the RPS. This obviated the need for monitoring during seed retrieval in the RPES, on formal exemption from the Radiological Council of Western Australia.

Both the immediate retrieval technique (QEII) and delayed retrieval technique (RPH) resulted in successful removal of all seeds without any seed damage. In the early phase of the project one seed was dropped during transfer to the Eppendorf tube. This was easily located on the floor using a scintillation counter and safely returned to Medical Physics.