Review

Synthèse

Appropriate procedures for the safe handling and pathologic examination of technetium-99m–labelled specimens

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This article has been peer reviewed.

CMAJ 2001;164(13):1868-71

Abstract

TECHNETIUM 99M MAY NOW BE USED TO IDENTIFY sentinel nodes for surgical excision in a growing number of cancer sites. The pathology specimens of these sentinel nodes and of any injected tumoural sites are radioactive. Consequently, specific clinical and laboratory procedures must be developed to handle these specimens safely. It is recommended that specimens containing the injection site should be quarantined for a period to permit decay of radioactivity. This quarantine does delay the reporting of pathology results to surgeons, oncologists and other clinicians, but it does not adversely affect final patient management.

The nodal status of patients with melanoma or breast cancer has usually been determined by en bloc resection of regional lymph nodes. This resection carries a significant risk of morbidity, identifies metastases in only a minority of patients and provides at best a small survival benefit.[1,2] The sentinel lymph node (SLN) is considered to be the first lymph node draining a tumour and is thus the first site of lymphatic nodal metastasis. Since SLNs are accurate in predicting the nodal status in the entire regional nodal basin, patients can be selected for regional lymphadenectomy on the basis of their SLN status.[1,3,4]

Previously, SLNs were identified using a blue dye (isosulfan blue) injected at the time of the surgery, but this technique used alone requires considerable experience and may involve substantial surgical dissection.[3] An injection of a technetium-99m–labelled sulfur colloid radiopharmaceutical in the tumour or scar site is now commonly used in addition to blue dye to localize the SLN, which is then detected using a hand-held gamma probe and direct visualization. Following selective resection of this node, the SLN is examined for pathologic evidence of any metastases.

The pathologic examination of the SLN is pivotal in the SLN procedure. If the node is positive, then regional lymphadenectomy is usually performed. If the node is negative, then unnecessary lymph node dissection and associated morbidity can often be avoided.[1,3] More sensitive immunohistochemical techniques increase detection rates of occult metastases and have been shown to be useful both in breast cancer and in melanoma.[4–6] Intraoperative (frozen section) examination or touch-preparation cytologic examination may be used to examine the SLN, which allows lymphadenectomy to then be performed during a single operative procedure and tissue to be preserved for final pathologic examination. The role of such intraoperative examination remains controversial, because false-negative reports of axillary SLN may deny the patient appropriate therapy.[2] Further research is needed to identify ways to improve the precision and accuracy of the pathologic examination of SLNs.[1,7] Furthermore, the ultimate clinical role and importance of SLN findings in breast cancer patients have yet to be defined. The clinical significance and implications to therapy of occult metastatic disease in lymph nodes that previously would have gone undetected need to be determined and are currently the subject of clinical trials.[4,8,9]

SLN assessment with ^{99m}Tc-labelled compounds is being introduced in many Canadian hospitals. Thorough training of surgeons and pathologists is required be-

fore the SLN procedures can be implemented.[7] Clinically node-negative T1 and T2 primary breast tumours and melanoma with vertical heights of 1 mm or greater are currently considered to be candidates for SLN biopsy at our institution. Indications for SLN procedures are extending beyond the original indications of melanoma and early breast cancer.[10] Research protocols for other cancer sites, including the vulva, colon and thyroid, are also underway or anticipated. Finally, ^{99m}Tc-labelled compounds may also be used to facilitate localization of parathyroids, and subsequent parathyroidectomy specimens will also be radioactive.

Hospital and laboratory staff, including surgeons and operating room staff, porters, imaging staff, and laboratory technologists and pathologists, must become familiar with the proper procedures for handling these radioactive specimens. Optimal procedures need to meet patient care requirements, ensure safe conditions for staff, comply with Canadian regulatory requirements and maintain laboratory efficiency.[6,7] Inadequate or poorly understood procedures could endanger the acceptance and elaboration of a novel and important surgical oncologic technique. Currently, however, there are no clear, well-defined guidelines for the handling of these specimens by clinical and laboratory staff.[11] Therefore, we have developed operating room and laboratory procedures that should be useful to other institutions as they choose to implement SLN surgery.

Sentinel lymph node assessment

Patients receive 40 MBq (about 1 mCi) of unfiltered ^{99m}Tc-labelled sulfur colloid at 140 keV with a radioactive half-life of 6 hours.[3] This colloid is constituted in 5–8 mL of saline for injections around breast tumours, or in 0.5–1.0 mL of saline for intradermal injection around melanoma sites. Patients are injected at the tumoural or scar site 2–4 hours before surgery, and they proceed to surgery after lymphoscintigraphy. Most of the ^{99m}Tc remains at the injection site, but a portion of it (perhaps 10%, or 100 μCi) will end up in the SLN. Radiolocalization is still accurate even after previous resection in breast cancer cases. If the tumoural site is to be resected, vital blue dye is also injected to aid in the identification of the sentinel node.

Exposure levels

The mean radiation dose to the hands of a surgeon performing SLN surgery in cases of breast cancer or melanoma is in the order of 9.6 (standard deviation [SD] 3.6) mrem (96 [SD 36] μSv) per operation, as measured by intraglove thermoluminescent dosimeters.[3] With these exposure levels, surgeons could perform thousands of operations annually without exceeding current US standards.[3]

Most of the SLN pathology specimens are radioactive, and this radioactivity is detectable for 16–48 hours after injection of the radiopharmaceutical.[3] In general, SLNs from melanoma patients are more radioactive than those from breast cancer patients, probably because the lymphatics of the skin efficiently carry the radiocolloid to the SLN.[3] Primary injection sites, which may be resected and submitted for pathologic examination, have significantly higher radioactivity than SLNs because about 90% of the radiocolloid remains at the injection site.

The radioactivity of the resected injection site or specimens from complete axillary node dissection is clearly present and measurable, but it poses a minimal health risk.[3,11] After measuring 18 specimens from 9 SLN and parathyroid cases, we found that the exposure dose equivalent rates at the time of specimen receipt from the operating room ranged from 0.1–18 μSv/h at the container surface. (For comparison, the total effective dose from a chest x-ray is 30 μSv.) These measurements confirm a previous estimate that the dose equivalent rates from SLN specimens among laboratory staff are 7.8 μSv/h.[11] Multiple specimens of SLNs and resection specimens stored together may result in a dose equivalent rate at contact of 30–60 μSv/h. The rate declines significantly over short distances. For example, it decreases to 1.5–4 μSv/h at 30 cm from the stored cases, which represents a better estimate of body dose. (For comparison, the dose equivalent rate at 30 cm from a patient immediately after injection for a bone or liver scan is 50 and 10 μSv/h respectively.) Furthermore, the ^{99m}Tc radiation is of low penetrance, and gloves provide substantial protection.

Nevertheless, laboratory procedures for the handling of ^{99m}Tc-labelled specimens must meet the regulatory expectations of the Canadian Nuclear Safety Commission (CNSC), formerly the Atomic Energy Control Board of Canada. Under its mandate, the CNSC regulates all radioactive materials in Canada through a licensing system. Licensees must use appropriate procedures for the acquisition, injection and control of all radioactive materials.[12] There are no specific regulations regarding radioactive specimens from patients, but CNSC standards are clear that specimens with radioactivity above 10 MBq cannot be handled in the routine manner for nonradioactive specimens. While ensuring that the benefits of new diagnostic technologies are available to the patient, laboratories must also maintain radiation exposure as low as reasonably achievable. Normal pathology procedures for specimens could lead to inadvertent or inappropriate handling, mailing, transportation or disposal of radioactive specimens. Specimens labelled with ^{99m}Tc do not have to be handled in laboratories designed to the specifications for handling basic radioisotopes,[13] but specific laboratory procedures for ^{99m}Tc-labelled specimens are needed. Our procedures for handling these specimens have evolved over the last year.

Handling procedures at our institution

In general, exposure to radioactive material is reduced if movement of the material is minimized, if the storage site of the material is shielded, if the area of use has limited and

controlled access, and if radioactive waste is appropriately handled. In addition, laboratories should have sufficient floor and work space and have surfaces that can be decontaminated if necessary.

In our institution, the operating suite (frozen section) laboratory is not designated as a radioactive laboratory, but surgical and pathologic procedures are performed there under an intrainstitutional permit under the appropriate consolidated CNSC licence. This permit designates this area and specific staff as being capable of working with ^{99m}Tc-labelled specimens. The laboratory is secured. Staff are required to wear whole-body thermal luminescence dosimeters. Potential radioactive contamination of work surfaces is monitored on a regular basis by conducting "wipe" tests. (A piece of filter paper moistened with distilled water is used to wipe the surface to be tested. The paper is placed in a scintillation vial, and radioactivity, if present, is measured on a scintillation counter.) A series of wipe tests may be performed on various areas of the laboratory. A log of the test results is kept.

Any ^{99m}Tc-labelled specimen containing the primary injection site (i.e., specimens containing the primary tumour or the excisional scar) are labelled in the operating room as being radioactive and then brought to the frozen-section laboratory by trained staff. Specimens containing SLNs or parathyroids have such low amounts of radioactive ^{99m}Tc that they are exempt from any CNSC handling requirements. Consequently, these specimens do not require radioactive labelling and, after the usual fixation, may proceed directly to the histology laboratory for routine processing. Applying the standard universal precautions for protection against exposure to body fluids and tissue, laboratory technologists and pathologists can perform any intraoperative touch-preparation cytologic examination or frozen section on either type of specimen if required for the intraoperative management of the patient.

The specimens containing the primary injection site are then placed in a container with formalin after slicing to ensure proper fixation, and they are quarantined for at least 24 hours in a shielded area to permit decay of the radioisotope. The length of quarantine may be shortened if additional radiation monitoring studies indicate that this is feasible. The shielded area consists of a simple lead-lined box placed on a shelf, although an acrylic plastic shield 1-cm thick may suffice. Any prepared slides are also placed into quarantine. Medical waste is discarded only after the quarantine has ended so that no detectable radioactive contamination of garbage occurs before final disposal into the regular garbage system. Since the cryotome does show measurable radioactive contamination following frozen section,[3] all tissue residue and shavings and all fluid-stained towels are disposed of in a garbage container labelled "radioactive waste" to allow decay before disposal with other tissue waste.

Following quarantine, specimens are no longer radioactive and can be forwarded to the histology laboratory to be handled in the usual fashion. The container's radioactive label is defaced at this time. In the histology laboratory, routine laboratory work flow (grossing, histologic processing, archiving and waste disposal) is maintained. Separate identification of what were once the more radioactive specimens (e.g., primary injection sites) is not necessary, and any residual tissue can be disposed of in the usual fashion. Any paraffin block handling (e.g., for mailing) can also be done in the usual manner. If a policy to quarantine specimens for radioactive decay is not adopted, special procedures must be devised for the safe handling of radioactive materials throughout the histology laboratory, which is a demanding, intensive task.[11] These special procedures would introduce inefficiencies into the laboratory.

Because of the need to place specimens containing the injection site in quarantine, surgeons and oncologists should expect some delay in receiving the final pathology report.[11] However, final patient management is not adversely affected.

Implementing procedures elsewhere

Many surgical services and laboratories across Canada will be expected to perform SLN procedures and pathologic examinations. Each service and laboratory must develop procedures for the safe handling of ^{99m}Tc-labelled specimens. These procedures might not be identical to our own, because different situations may require different protocols to meet patient care, CNSC regulations and staff expectations. Increased experience with this new technique may lead to changes to these outlined procedures. Currently, however, these considerations and procedures are a useful guide for laboratories as more and more surgeons adopt the use of SLN surgery.

Addendum

Since the acceptance of this manuscript, recommendations have been published for the handling of radioactive specimens obtained through sentinel lymphadenectomy.[14] The document discusses the issues from an American perspective, and many of the recommendations are similar to those contained in our article, with some exceptions. In our opinion, our recommendations are optimal in that laboratory workflow efficiencies provided by the quarantining of primary resection specimens are maximized.

Competing interests: None declared.

Contributors: Terence Colgan identified the handling of technetium-99m–labelled pathology specimens as a potential problem, researched the issue and developed a consensus regarding appropriate procedures. Diana Booth considered the technical aspects of the procedure. Aaron Hendler and David McCready oversaw the introduction of ^{99m}Tc-labelled SLN methodology in the University Health Network and assisted in the development of these clinical and laboratory procedures.

Acknowledgement: We thank the staff of the University Health Network's Radiation Safety Office, in particular Ms. Gina Capone and Mr. Frank Tourneur for their insights into regulatory issues and their cooperation in the development of these procedures.

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