Evolving roles for oncology nurses: Biospecimen collection

The personalized oncology revolution hinges importantly on determining and monitoring tumor and patient genetics and molecular biomarkers that can guide targeted therapy. The oncology nurse is frequently responsible for collecting, preparing, and often, managing, the biospecimens needed for these analyses.

As molecular tests have proliferated, the “complexity, required knowledge, and expectations of the oncology nurse have changed dramatically over the past decade,” says Sharon Kaufman, MS, a research protocol specialist at the Mayo Clinic Cancer Center in Rochester, Minnesota.

“Many cancers are caused, at least in part, by several different genetic mutations along several different metabolic pathways,” Kaufman and coauthors noted in a recent review on oncology biospecimen collection and processing.1 These mutations and their gene products can be inhibited by targeted molecular therapies, at least temporarily.1 A goal of personalized oncology is to develop such targeted therapies and deploy them strategically against tumors with specific vulnerabilities. Toward that end, and to develop better risk-stratification tools, myriad prognostic biomarkers derived from blood and tumor tissue exist and are under development.1,2

Educating patients about the purpose of these tests, and collecting and preparing biospecimens with which to perform them, frequently fall within the responsibilities of the oncology nurse. “Oncology nurses used to monitor vital signs and administer chemotherapy,” Kaufman tells *Oncology Nurse Advisor*. “Now, they [also] need to be experts in collecting and processing blood and tissue; dissecting clinical trial protocols to determine the details of collecting and processing; helping guide patients through their treatment options, clinical trial options; and then monitoring vital signs and administering chemotherapy.”

Oncology nurses must familiarize themselves with biomarker analyses relevant to their patients, biospecimen collection techniques for biomarker analysis, and not least, institutional policies, standard operating procedures, and laboratory manual guidance.

Increasingly, effective treatment planning and monitoring require detailed insight into the tumor's molecular biology and genomics. Circulating tumor cells can now be captured and isolated for genetic analysis and determination of a tumor's suitability for targeted therapies, a process sometimes called *liquid biopsy.*

“A few decades ago, a drop of blood was used to determine blood type, biopsies were believed to enhance the likelihood of metastases, and nursing assessment for a person believed to have cancer was limited to palpation and examination of [radiographs],” noted Kaufman and coauthors.1 Those ideas have changed. Today, that drop of blood provides much more information; it essentially opens a window into a person's genetic makeup and risk profile.

Biopsy specimens can be subtyped not just by histology, but tumor genetics and epigenetics for targeted therapy and stored for future research use as well. Nurses are expected to coordinate the correct collection of blood and tissue; mediate the overlapping needs of the clinical and research teams; then navigate patients through a maze information systems that will help them understand risk, diagnosis, and treatment data at an individualized level.1

## BLOOD COLLECTION

Collection tubes are typically 10 mL; coagulation tubes, used to collect samples for coagulation determination, are typically 4 mL.1 “There is some good news here,” says Kaufman. “Advances in the tests and assays themselves have allowed smaller and smaller volumes for testing, into the range of nanograms.” That should translate to smaller and smaller blood volumes in the coming years.

Written protocols or lab manuals should be reviewed prior to a blood draw for specific requirements associated with a given test. Given the rapid accumulation of new biomarkers and tests, the updating of lab manuals represents a conundrum, cautions Kaufman.

“Typically, the lab manual does not require IRB [Institutional Review Board/Human Subjects Review Committee] review and can be changed relatively easily,” she notes. “That's fine when administrative details need to be updated. However, if something in the lab manual changes that affects the protocol or budget—volume of blood, ultrasound guidance for a biopsy—then it should be subject to review.”

Depending on the intended analysis, the blood collection tubes will contain anticoagulants or preservatives, as indicated by color-coded caps.1 Red tube caps typically indicate no additives, such as those used for identifying antibodies, immune proteins, or lipids; whole-blood coagulation tubes have light blue caps; lavender or royal blue caps contain clot-preventing EDTA for complete blood counts and DNA extraction for genetic mutation analysis; gray-capped tubes contain sodium fluoride to preserve glucose and allow electrolyte analysis; and green-capped tubes contain heparin to prevent clotting for rapid blood chemistry labs.1 Yellow/purple (bicolored tiger-striped) tube caps usually represent collection tubes for circulating tumor cell (liquid biopsy) analyses of cancer genomes and genetic mutations.1 Close attention to collected volumes is necessary, particularly as a collection tube's expiration date approaches and tube vacuums grow weaker, resulting in incomplete filling.1

Blood collection supplies should be organized and reviewed before placing the tourniquet, Kaufman and coauthors emphasize.1 “(T)he longer the tourniquet is in place, the higher the risk of hemoconcentration of nonfilterable elements such as proteins in the blood,” they explain.1 “If the blood must be drawn from the same arm as an intravenous access site, then the tourniquet must be placed several inches above the site and only tight enough to restrict superficial venous flow. Tourniquets should not be left in place longer than 2 minutes before being loosened.”

Once filled, blood collection tubes are completely inverted gently and repeatedly, typically five to 10 times. One inversion involves turning the tube completely upside-down (180˚) and back to cap-end-up1 (**Table 1**). If the protocol calls for clot formation within the tube, the tube is left at room temperature for a minimum of 30 minutes.1

**TABLE 1. Tube handling for blood collections1**

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| **Tube/syringe order of draw** | **Number of inversions** |
| Plain syringe | None |
| Royal blue (plain metal) | 5 |
| Special coag (screw cap) | 3-4 |
| Blue | 3-4 |
| Black | 3-4 |
| CAI (SST) | 5 |
| Gold (calcium & other SST) Red RST | 5 |
| Green Mint green | 8-10 |
| Royal Blue (EDTA metal) | 8-10 |
| Purple Pink Black/tan tiger (sequenom) | 8-10 |
| Cellsave (purple/yellow) | 8-10 |
| Gray | 8-10 |
| Yellow | 8-10 |
| Pyruvate (screw cap) | Shake vigorously 10 times |
| QTB tubes (3) | Immediately after filling tubes, shake 10 times just firmly enough to coat tubes |
| PAXgene (RNA) | 10 |
| Lithium heparin syringe | Mix the sample horizontally for 30 seconds and then invert several times |
| **KEY:** CAI, free ionized calcium; EDTA, ethylene diamine tetra acetate; RNA, ribonucleic acid; SST, serum separation tubes. | |

Processing collected blood samples may also include centrifuge spinning at specific speeds and durations to precisely fractionate the sample into readily visible layers, with red blood cells at the bottom, above which will be found white blood cells and plasma on the top, respectively.1Carefully following written protocols' specific guidance on centrifuge timing and speed is crucially important to avoid degrading the blood sample, as incorrect timing can leave blood components inadequately separated or damage blood cells.1 After a sample is centrifuged, the layers are collected with a pipette into separate tubes for subsequent analysis. Naturally, each sample must be carefully documented.

## TISSUE COLLECTION

Tissue biopsy processing for analysis is evolving, with a trend away from the once-common formalin-fixed paraffin embedded (FFPE) preservation of biopsy tissue for future analysis to flash-freezing freshly harvested samples in liquid nitrogen and storage at –80˚C. Biopsy tissue samples should not exceed 0.5-cm dimensions, and regardless of whether preservatives are used, both preservation and freezing must occur rapidly.1

“Paraffin-embedded tissue seems to be of lesser quality, particularly where extraction of DNA and/or RNA is concerned, requiring a level of skill on the part of the lab personnel that is rare,” Kaufman explains. Fine-needle collection of tumor tissue and cells is also common.1

The timing of postcollection processing for preservation is key, and all equipment must be ready before collection begins.1 When collecting samples from resected surgical specimens, the time from when blood flow to the tissue is clamped off to the time of flash freezing or immersion in formalin should be minimal.1 Frequently, particularly when a patient is participating in a clinical trial, tissue sample preparation may need to follow precisely specified procedures for specific biomarker analyses.

“I don't believe that any of the collection and processing techniques are particularly difficult,” Kaufman says. “The challenge is doing it all within the protocol-specified time frames, which are all different. It's more and more common that these details are so specific that they cannot be written into the protocol. A lab manual is then required.”

For example, collecting tissue during a colonoscopy or bronchoscopy is a matter of being in the room, explaining to the clinician performing the procedure as to what to collect and from where, then accepting the tissue sample provided.

“If there are eight pieces of tissues, they'll likely come in rapid-fire succession,” Kaufman explains. “Some will have to be put into cryo-vials and immediately placed into liquid nitrogen. Some will be put into a container with formalin. For the latter, the protocol will specify how long the tissue has to be in formalin before it's embedded in paraffin.”

If paraffin blocks cannot be used, then slides are made from the paraffin block. “The nurse will have to navigate the institutional policies, arrange for paraffin embedding, and arrange for cutting slides, usually in a histology lab.”

All cancer clinics should have written standard operating practices (SOPs) for these procedures. Even in clinics that do not participate in clinical trials, blood and tissue samples need to be collected for assays and gene sequencing that will likely guide the course of treatment for many patients with cancer, explained Kaufman.

## THE FUTURE

With the increasing emphasis on biomarkers in treatment planning and monitoring and as biospecimen collection become more voluminous, many cancer centers may consider employing biospecimen resource managers. To date, many institutions tend to expect its oncology nurses to take on that role or have assigned others to become specialists/managers for biospecimen collecting.

“However, there's more involved than just assigning a person to manage the biospecimens,” Kaufman cautions. Quite a bit of infrastructure is also required, including laboratory facilities, freezers, storage—and *policy* for accessing clinical archives for research, the approvals required, and biospecimens and biosafety review committees.

Understanding cancer at the molecular-genetic level will lead to detailed diagnoses and precise treatment planning, Kaufman and coauthors predict.1 “Among the emerging responsibilities of the oncology nurse is helping patients to take control of their disease and treatment.”

“Once again, the oncology nurse will need to be a navigator,” Kaufman explains—a role that is itself undergoing a transformation in the era of personalized oncology care. “The role of navigator has changed from helping the patient navigate the possibilities for cancer treatment, to helping the patient navigate ethics, genetics, prevention options, family history, and costs.”

One often-neglected facet of personalized oncology is the availability to individual patients of independent whole-genome sequencing with a single blood draw, at a cost of approximately $1,000. “This provides the patient with a huge amount of information but very little context and no truly reliable interpretation,” Kaufman warns. One of the emerging roles of the oncology nurse will be to help patients evaluate their probable risks based on genetic, lifestyle, and other factors.

“The science is changing very quickly,” Kaufman notes. “Oncology nurses have always had to participate in continuing education. It now more critical than ever.”

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