NCCCP Biospecimen Initiatives

Bringing Research Advances to the Community Setting

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The National Cancer Institute Community Cancer Centers Program (NCCCP) was launched in 2007 as a three-year pilot, forming a public-private partnership with 16 community hospitals to explore the best methods to enhance access to care, reduce healthcare disparities, improve quality of care, and expand research within the community setting.[1] At the conclusion of the pilot period, the network sites collaborated to produce White Paper reports to document their experience addressing program deliverables in specific focus areas. *Oncology Issues* introduced a series about the NCCCP White Papers in the January/February 2011 edition.[2] This issue features content from the Biospecimens Subcommittee White Paper.

Given changes in science and technology that are driving discoveries in the study of cancer and its treatment, an objective of the NCCCP pilot was to understand the capacity for community hospitals to collect high-quality biospecimens and thus bring research advances to the community setting and partner with NCI and its research mission. High-quality biospecimens are critical for molecular research, the foundation for developing molecularly targeted therapies. NCCCP's efforts involved understanding how to prepare NCCCP sites for consenting donors, collecting, processing, annotating, and storing specimens in biorepositories and/or distributing them to other laboratories or biorepositories. The experiences of the pilot sites were detailed in the NCCCP Biospecimens Subcommittee White Paper; highlights from the paper follow.

NCI began a due diligence process in 2002 to formally develop standardized resources for biospecimen research. The recommendations for standardizing biorepository protocols were released in 2003 via publication of the National Biospecimen Network Blueprint and Case Studies of Existing Human Tissue Repositories. In 2007 NCI created its NCI Best Practices for Biospecimen Resources (*NCI Best Practices*), which promoted state-of-the-art guiding principles to optimize biospecimens for cancer research. The document contained guidelines for informed consent, biospecimen collection, annotation, storage, and distribution. It also included guidelines for data gathering and recommendations for dealing with ethical and legal issues arising from biospecimen care and research. Based on comments from the biospecimen resource community, as well as more current and scientifically accurate recommendations, NCI revised the document in 2010. The document is available online at: *http://biospecimens.cancer.gov/practices/2010bp.asp*.

In 2007 the pilot sites reviewed the *NCI Best Practices* to determine the necessary requirements for their community hospitals to implement NCI objectives for research biorepositories. The NCCCP Biospecimens Subcommittee set the following goals:

- Complete the Biospecimens Gap and Fill Assessment Tool
- Address biospecimen formalin-fixation best practices (see page 34)
- Address disparities initiatives through a Special Request Biospecimen Disposal Standard Operating Procedure (see page 38)
- Establish a medium for external speakers to provide best practices to participating NCCCP sites
- Work with NCCCP sites on their local biorepository initiatives and document the various approaches.

Biospecimen Program Assessment

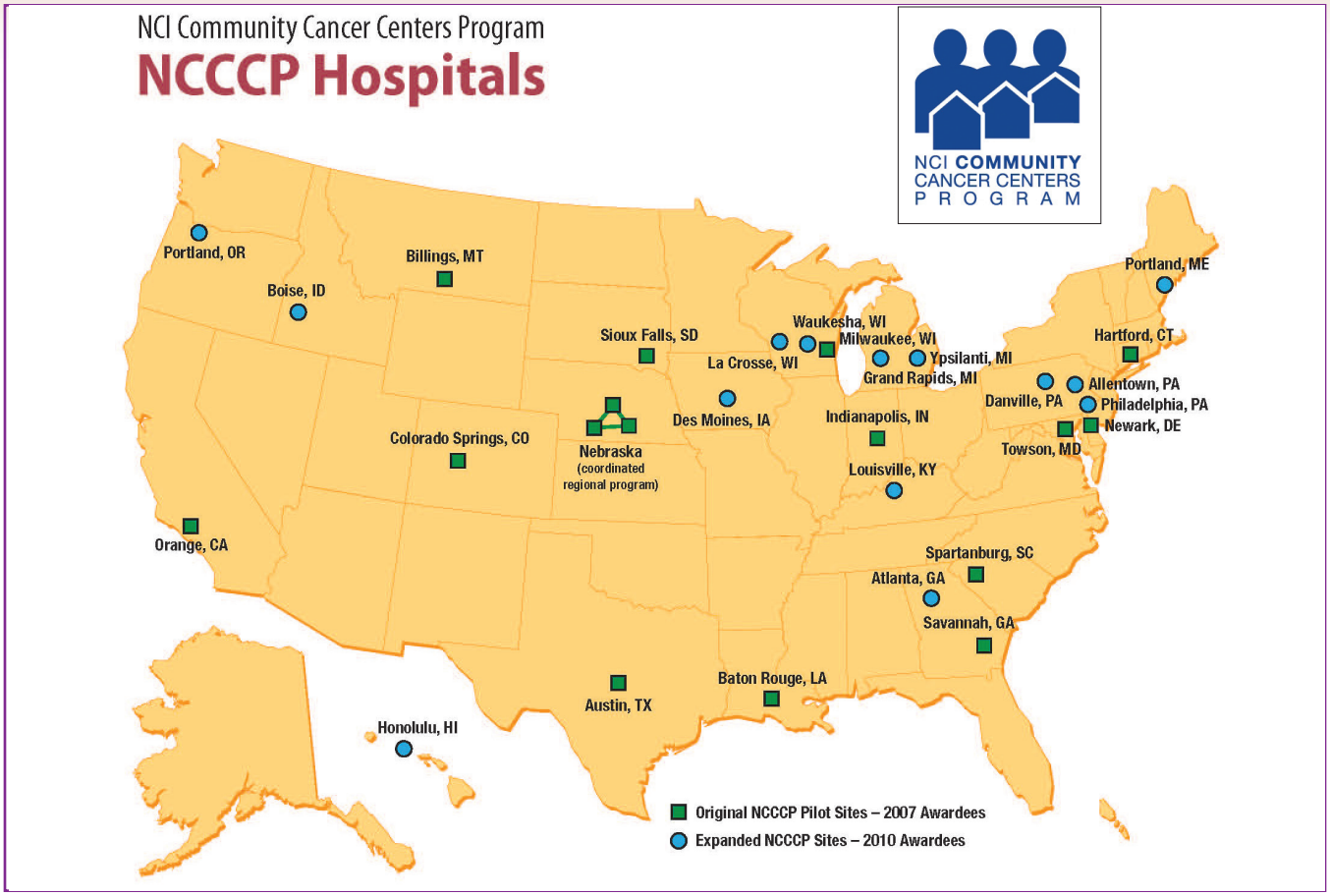
At the start of the NCCCP pilot, each site was responsible for evaluating and documenting the current state of its biospecimen program. To help in this effort, the Biospecimens Subcommittee created a Gap and Fill Assessment Tool (GAFAT). The sites used this tool to identify both current gaps in their biospecimen programs and solutions (or "fills") to those gaps. Based on the *NCI Best Practices*, the GAFAT served as a guide for tissue handling from all patient tumor resections for both clinical care and research purposes. Pilot sites initially completed the GAFAT in June 2008 and then updated it for final completion in fall 2009. The assumptions were: 1) to include all cancer resections for patient care and research and 2) that sites had access to unlimited resources (i.e., personnel and funds). The GAFAT addressed many competencies, including:

- Biospecimen consenting, annotating, collecting, processing, storing, and distributing
- Quality assurance and quality control
- Biosafety
- Principles of responsible custodianship
- Privacy protection
- Intellectual property.

The GAFAT used by the pilot sites had three tiers, with each tier divided into the following two portions for sequential use:

- Scope, Applicability, Implementation, Technical, and Operational Best Practices
- Ethical, Legal, and Policy Best Practices.

Completion of the GAFAT tool was an NCCCP deliverable, but more importantly, this process added value to sites



through the evaluation of their capabilities for proper handling of biospecimens. The GAFAT also helped to show sites' capacity to support and participate in clinical trials that include a tissue collection component. Several sites voluntarily used a Biospecimen Percentage Implementation Tool (BPIT), an Excel spreadsheet, to track the progress of "fills" implementation on a quarterly basis.

Key Stakeholders

Support and engagement of key stakeholders was essential to successful implementation and use of the GAFAT. Assessment, development, and implementation of a biospecimen plan encouraged collaboration between oncology research professionals, information technology, and pathology departments for subsequent implementation of best practices in handling of biospecimens. At the NCCCP pilot sites, many individuals from the pathology laboratories provided insight for and collaborated on the development of the GAFAT, including pathologists, pathology assistants, tissue bank staff (if existing biorepository), histotechnologists, and medical technologists. Ethicists and members of the legal department also participated by ensuring that solutions to fill the GAFAT complied with all ethical and legal standards.

Even with stakeholder buy-in and support, the GAFAT document was laborious and required extensive education about its use, utility, and data requirements. NCCCP sites reported that the tool was cumbersome and time consuming in the early phase of implementation. This challenge was eventually resolved through further education, site-pairing, and process mentoring.

Strong collaboration among the network sites and NCCCP leadership was critical to enabling individual sites to meet program objectives. Site-pairing (i.e., matching sites with more biorepository experience to sites with less experience) afforded opportunities for best practice sharing. In addition, the ongoing presence of a "site champion" for this project helped guide the development and implementation process for the GAFAT. These combined efforts, along with ongoing education, were critical components to the successful implementation and use of the GAFAT. Once in place, the tools provided an accurate measure of sites' baseline and progress, and helped guide the future direction of NCCCP biospecimen initiatives.

Updating the Tools

Information learned during NCCCP's three-year pilot period and updates made to the *NCI Best Practices* in 2010 led to modifications of the GAFAT-BPIT. The Biospecimens Subcommittee developed a simplified version with formulas that streamlined use and improved quantitative analysis. When the NCCCP network expanded from 16 to 30 sites in 2010, the revised tool was approved for use and its completion became a baseline deliverable for all 30 sites. The GAFAT-BPIT is now being used as a quarterly report tool to follow the overall progress of NCCCP sites.

References

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[2]Johnson M, Clauser S, O'Brien D, Beveridge J, Kaluzny A. Improving cancer care and expanding research in community hospitals. *Oncol Issues.* 2011;26(1):26-28.

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NCCCP Site Participation in the Formalin Fixation Project

Adequate tissue fixation is essential not only for preserving cellular morphology and diagnosing cancer, it is also critical for the accurate identification of protein profiles and molecular nucleic acid signatures used to personalize prognosis, prediction, and therapy for patients with cancer. Very little standardization of tissue fixation exists among pathology laboratories in the United States and elsewhere. Although non-formalin fixatives have been used in diagnostic pathology, 10% phosphate-buffered formalin without "proprietary additives" remains the "gold standard" for tissue fixation and diagnostic immunohistochemical (IHC) testing.[1] Studies have also shown that development of RNA-based assays from formalin-fixed, paraffin-embedded tissue is feasible; however, greater attention to tissue handling and processing is essential to improve the quality of biospecimens.[2]

In 2007 the American Society of Clinical Oncology (ASCO) and the College of American Pathologists (CAP) published recommendations for HER2/neu testing in breast cancer.[3] This pivotal paper recommended that breast tissue be fixed in formalin for at least 6 hours and no longer than 48 hours. More recently, ASCO and CAP published the complementary Estrogen Receptor/Progesterone Receptor Guideline that updated the total time in formalin to between 6 and 72 hours.[4]

In January 2009 the NCCCP Biospecimens Subcommittee initiated discussions on best practices for the collection, fixation, and processing of biospecimens for IHC and molecular testing. Participation in the formalin fixation project was voluntary. Although not an NCCCP subcontract deliverable, sites agreed to collect this information to establish a baseline for community hospitals' capabilities to follow *NCI Best Practices.* The intent was to establish protocols that would allow pathology laboratories to provide "high-quality" biospecimens for histologic diagnosis, molecular research, and construction of targeted therapies for patients with cancer.

The 2007 ASCO/CAP HER2 guideline and a working draft of the ASCO/CAP ER-PgR guideline served as the foundation for developing and implementing NCCCP's formalin-fixation best practices for the collection and preservation of tissue biospecimens.[4]

Development and Implementation of Formalin Fixation Best Practices

The Biospecimens Subcommittee provided a forum for sharing ideas and strategies for the implementation of the best practices based on the experiences of the participating NCCCP sites, and then allowed for benchmarking progress among the sites. Stakeholders included pathologists, laboratory staff, and pathologist assistants. It was essential to develop cooperation with a wide range of hospital departments and clinicians, including surgeons, medical oncologists, radiation oncologists, interventional radiologists, anesthesiologists, and others. The rationale for NCCCP site participation was that the development of infrastructure at local sites could support the collection of high-quality biospecimens for enhanced patient care.

Formalin fixation time is calculated from the time the biopsied or dissected (from resection) specimen is placed in formalin until the time it is removed from formalin, including the time in formalin during processing. A 6 to 72 hour formalin fixation time was mandated. This required the following:

1. The cooperation of the pathology department and the nursing/OR staff
2. Education on terminology
3. Revision of the pathology specimen requisitions.

A change in tissue preparation workflow (e.g., specimen cut-off times and weekend coverage) was necessary to ensure appropriate fixation times.

To develop the process at NCCCP sites, standard data elements were included in pathology reports, such as "Formalin fixation time is 6 to 72 hours" or "Total time in formalin is _____." The data to calculate total time in formalin include date and time specimen is placed in formalin and date and time specimen is removed from formalin. The first datum point (date and time placed in formalin) is provided by the clinician and/or OR staff or, in some instances, the pathology department if the specimens are received fresh. The second datum point (date and time removed from formalin) is determined by the pathology department. The actual times could be maintained on the specimen requisition or on the report, but were not required on the final reports.

Implementation at some NCCCP sites required a new mindset regarding turnaround times of surgical specimens to accommodate for appropriate fixation times. A few sites had to make weekend staffing changes. The ASCO/CAP guidelines for reporting predictive markers in breast carcinoma were used to educate staff about requirements that made these changes necessary. Several of the sites added templates for reporting the fixation times on the pathology reports to laboratory information systems; other sites developed programs for fixation monitoring. Sites trained pathologists and histology staff on placement of tissue in the appropriate processors with specific programmed times in formalin.

Success was monitored by the reporting of "formalin fixation time" on the pathology report—another requirement of the more recent ASCO/CAP guidelines. This requirement was instituted predominantly for breast carci-

noma cases, with some NCCCP sites planning to include fixation times on all pathology reports.

Pathology assistants monitored requisitions for the appropriate data elements. Histology managers worked closely with the OR staff leadership to ensure success. When documentation was not present, communication by phone or email between the pathology and histology staff and the OR staff ensured timely feedback and correction of any deficiencies.

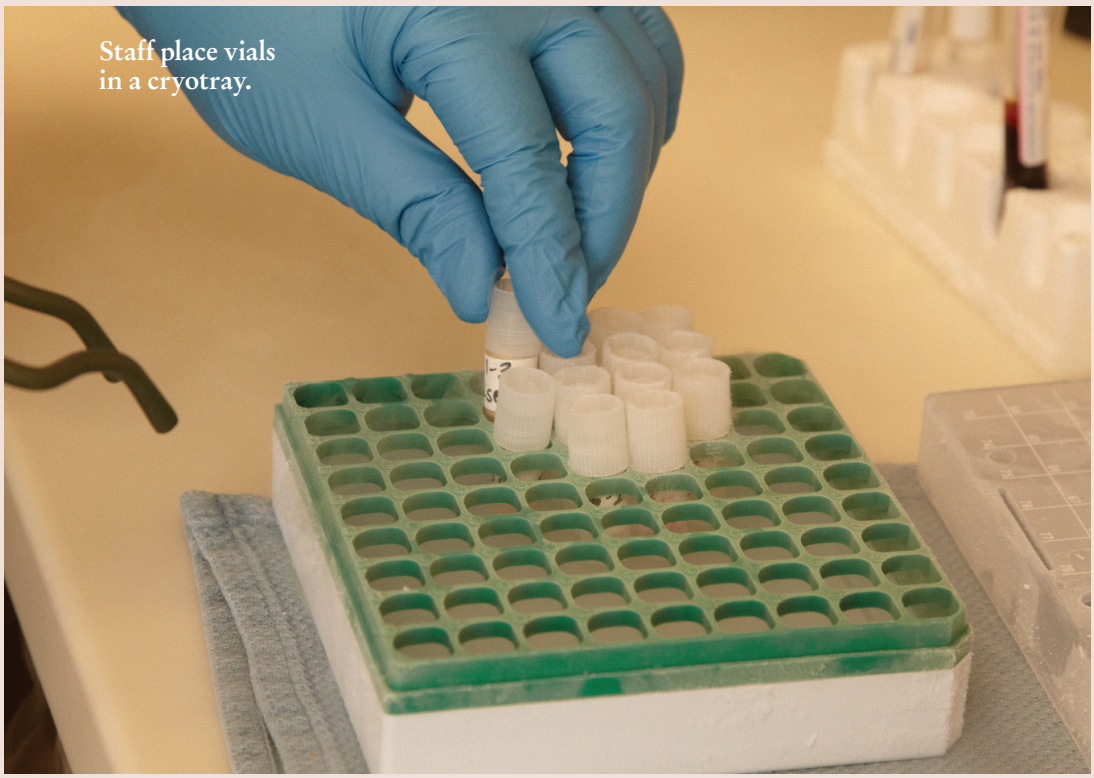
While implementation of changes to ensure 6 to 72 hour total time in formalin became part of the normal work flow at NCCCP sites, barriers to the process included:

- Lack of understanding of the critical nature of the process by OR staff and OR technicians
- Competing priorities, such as specimens delivered fresh for intraoperative consultation or frozen section
- Tissue processors that may require different start times for standardization of time in formalin
- Commercial anatomic laboratory information systems (LIS) in the community currently do not have searchable fields for formalin fixation times and are not easily customizable for this feature; therefore, additional work was needed for the pathology assistants to dictate times and for the transcriptionists to type the data.

NCCCP sites provided educational tools to support the implementation of standard fixation times. For example, the Biospecimens Subcommittee offered presentations on the scientific significance of fixation time, focusing attention on the molecular process of fixation. The subcommittee also audited NCCCP sites for adherence to best practice fixation times by requesting percentages of specimens fixed within the 6 to 72 hour time interval as a deliverable. Data from early in the process and during implementation allowed sites to benchmark with other community hospitals.

Implementation of the 6 to 72 hour "formalin fixation time" requirement varied greatly among NCCCP sites. Several pilot sites started with policy and procedure development while other sites already had policies in place.

Costs to incorporate these process changes were not measured at any of the NCCCP sites. Associated costs may include education time of staff, reprinting requisitions, staff time to document data elements, and time for pathology assistants to dictate information. A potential cost is modifications to the LIS that would help with time calculations and provide automated recording of data on reports and audits. Implementation of LIS changes may help decrease the staffing costs to provide these data, especially if defined fixation times are required on all specimen types.



Staff place vials in a cryotray.

Lessons Learned and Recommendations

While many pathology laboratories have adopted the ASCO/CAP recommendations for formalin fixation of breast specimens, it is important to note that these are not "mandates." Although the ASCO/CAP recommendation for a minimum of 6 hours of formalin fixation was based on a study by Goldstein and colleagues[5] that looked at estrogen receptor staining in invasive breast carcinoma, an earlier study examining the effect of prolonged formalin fixation on breast biomarkers found that HER2/neu was stable for up to 20 days and ER/PR staining for up to 57 days.[6] Therefore, individual laboratories are free to use alternative fixation guidelines as long as they validate their protocols against the recom-

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mended guidelines. In addition, while the NCCCP focused largely on formalin fixation times, delay to fixation (cold ischemia time) may have a negative impact on the identification of biomarkers. The recent ASCO/CAP ER-PgR guideline recommends that the delay to formalin fixation not exceed one hour and that biospecimens not be stored overnight at 4° C prior to fixation.[7]

Participating NCCCP sites conducted formalin fixation studies in 2009 and 2010. Study results indicated that laboratories in 2009 were able to calculate formalin fixation times in the majority of breast specimens, and 2010 data suggested that formalin fixation documentation was improved on all case types.

Many factors led to success among the different NCCCP sites challenged with maintaining and recording formalin fixation times. Communication, cooperation, and collaboration among multiple service areas, based on the knowledge that there is good scientific rationale for changing practice, proved important. Sites had to determine how to efficiently accomplish the goal of implementation within the context of limited resources (see "Steps to Implement Formalin Fixation Times at an NCCCP Site" at right).

The Biospecimens Subcommittee recommended ongoing educational events for the NCCCP network sites. With increased emphasis on formalin fixation studies, the goal for continued education is to break barriers to practice changes, improve tissue handling procedures, and implement changes in the community hospital setting that will advance molecular research to support genomically informed medicine.

References

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[2]Hewitt SM, Lewis FA, Cao Y, et al. Tissue handling and specimen preparation in surgical pathology. Issues concerning the recovery of nucleic acids from formalin-fixed, paraffin-embedded tissue. *Arch Pathol Lab Med.* 2008;132:1929-1935.

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Fixation Time Documentation

Diagnostic pathology laboratories are tasked to keep track of the exact time that a breast biospecimen has been fixed in formalin and the 2010 ASCO/CAP ER-PgR guideline requires that this information be included in the surgical pathology report.

An alternative approach, based on the process set up at an NCCCP-hospital-affiliated laboratory, is recommended for those laboratories that find it difficult to document the exact time of fixation: Once minimum and maximum fixation time guidelines were established by the individual laboratory, a policy was established that ensured all breast biospecimens satisfied the fixation requirements. For example, if a laboratory follows the 2007 ASCO/CAP "6 hour" minimum fixation recommendation, then the combined time of "pre-tissue processor" and "tissue processor" formalin fixation must add up to 6 hours. Therefore, it is necessary for the surgeon, interventional radiologist, and pathology staff to document the FCT (time biospecimen is placed in formalin) on the pathology requisition for all breast biospecimens. Knowing the FCT and when the tissue processor is started, a decision would be made as to whether the biospecimen is set-up that day or held until the next day for processing. Continual surveillance of FCT compliance should occur and feedback be given to those individuals not documenting the FCT for their patient's biospecimen.

While achieving the fixation time goal was a challenge for NCCCP sites with limited resources, all sites felt their accomplishments far outweighed the challenges. Most sites gained compliance with the ASCO/CAP guidelines and expanded the process from breast tissue to all or most tissue types with the knowledge that patients benefit from optimally processed tissue. It has been suggested that as implementation of the *NCI Best Practices* continues to grow, documented FCT may be necessary for other types of cancer that require immunohistochemical and/or molecular studies for diagnosis, prognosis, or research.

Other obstacles were encountered primarily when NCCCP sites had to change long-established processes. Workflow in the histology labs needed adjustment to accommodate for the minimum 6 hour and maximum 72 hour specimen fixation times. Simple changes included training staff to calculate fixation times. A web-based calculator was identified for use. The tool is available online at: *http://www.timeanddate.com/date/timeduration.html*).

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that will advance molecular research to support

Steps to Implement Formalin Fixation Times at an NCCCP Site

- ✔ Meet with hospital committee (Cancer Care Committee) to initiate working group.
- ✔ Educate working group on significance of initiative.
- ✔ Revise requisition and ordering process to include date/time of removal of specimen(s) on all cases and date/time formalin added.
- ✔ Educate OR staff and other hospital areas that submit biopsies to include time of removal and time formalin added.
- ✔ Educate pathology assistants and pathologist to document time formalin added on cases sent fresh or for frozen sections.
- ✔ Use training tools/signs in OR and outpatient surgery areas and radiology.
- ✔ Determine time out of formalin on all processors in histology department. Develop a chart based on what time tissue is placed in formalin will allow for appropriate time in fixation (6 to 72 hours). Load processors appropriately.
- ✔ Develop canned text to be placed on all reports to indicate fixation time. Example: Pre-analytic factors: Time in 10% phosphate-buffered formalin is between 6 and 72 hours. Pre-analytic factors: Time in 10% phosphate-buffered formalin is greater than 72 hours (74 hours, 10 minutes).
- ✔ Train histology staff to calculate the time with aid of online time and date duration calculators and to indicate which canned text to use.
- ✔ Train transcriptions to enter canned text codes from times/codes as documented by histology staff.
- ✔ Monitor process. Identify locations not providing times appropriately for further education. Surgeons/OR may need to be educated to not leave specimens in OR without formalin until case finished.
- ✔ Develop methods to calculate overall formalin fixation rates.
- ✔ Work with anatomic pathology laboratory information systems to allow for time entries, calculations, and automated documentation.

In the future, hopefully, nationally recognized LIS companies will automatically include solutions to include time to decrease the manual calculations, coding, and transcription.

PHOTOGRAPH/ISTOCKPHOTO

testing in breast cancer. *Arch Pathol Lab Med.* 2007;131:18-43.
[4]Hammond MEH, Hayes DF, Dowsett M, Allred DC, Hagerty KL, et al. American Society of Clinical Oncology—College of American Pathologists Guideline Recommendations for Immunohistochemical Testing of Estrogen and Progesterone Receptors in Breast Cancer. *J Clin Oncol.* 2010;June 1;28(16):2784-95.
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Developing a Special Request Biospecimen Disposal SOP

A core goal of the NCCCP is to reduce cancer healthcare disparities. An early step in the process is to understand the diverse populations that are cared for, beginning with the study of biospecimens collected for cancer research. Personal, religious, and cultural beliefs can affect an individual's decisions regarding biospecimen disposal or return; therefore, it is important to have policies for the handling of biospecimens that are congruent with the religious and cultural beliefs of the populations served.

Disposal SOP Development and Implementation

The NCCCP Biospecimens Subcommittee developed the NCCCP Special Request Biospecimen Disposal SOP in an attempt to responsibly handle requests related to biospecimens collected from individuals of different cultural backgrounds and ethnicities. The model was based on the protocol at Billings Clinic and the College of American Pathologists (CAP) Guidelines. The generic SOP template was designed to be respectful of the communities served by the NCCCP with the intent of ensuring a mutual understanding of processes for biospecimen handling between pathology custodians and patients who have cultural and/or religious beliefs about human tissue. The subcommittee created the template to help NCCCP sites: 1) encourage and assure patients who might otherwise limit their participation and 2) foster patients' trust that their wishes will be honored.

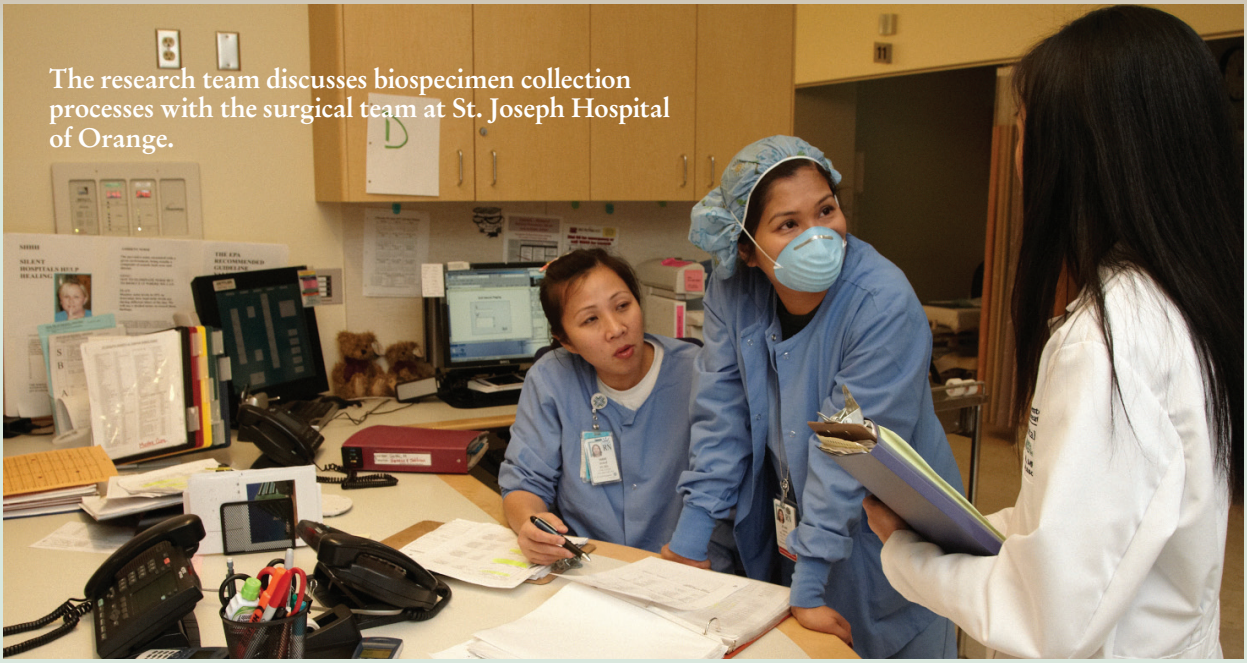
Development of the disposal SOP template involved many participants from various NCCCP sites, particularly in the research and biospecimen fields. Stakeholders in the Disparities, Clinical Trials, and Biospecimens Subcommittees were engaged, and site-specific ethics and legal staff were critical to defining issues relevant to such a protocol and ensuring that it could be effectively implemented at NCCCP sites. Tissue procurement staff was also engaged in the process, which allowed for a thorough discussion of the options available to accommodate various religious and cultural beliefs. In addition, pathologists and others involved in tissue processing were consulted to ensure that tissue could be safely returned after processing without causing any increase in risk of cancer (because of the formalin) or becoming biohazardous if someone then chose to dispose of the tissue in an unapproved manner.

The Special Request Biospecimen Disposal Protocol SOP template includes:

1. A Biospecimen Disposal Standard Operating Model Procedure for Special Requests Outside the Scope of Routine Biospecimen Disposal Policy (page 40).
2. A Model Biospecimen Special Disposal Request Form (page 41).
3. A Model Biospecimen Special Disposal Release Form (page 41).

During the protocol development and implementation process, the NCCCP pilot sites shared best practices and created a process that was "friendly" to the community hospital setting. While special requests for biospecimen disposal may not arise often in some areas of the country, NCCCP sites needed to be prepared to address the issue. The Biospecimens Subcommittee circulated the SOP to NCCCP sites to gather comments and suggestions from those that serve diverse cultures, as well as to ensure buy-in for future site adoption. Very early involvement of the pathologists and medical and surgical sub-specialists involved with tissue procurement was helpful to successful implementation of the SOP.

Biospecimen tissue collection during a surgical procedure at St. Joseph Hospital of Orange.



The research team discusses biospecimen collection processes with the surgical team at St. Joseph Hospital of Orange.

Lessons Learned

NCCCP sites reported the following challenges to the Special Request Biospecimen Disposal SOP:

- Competing priorities that prevented project completion
- State and local laws that required release of biospecimens through a mortuary
- Low frequency of special requests.

By the end of the NCCCP pilot's third year, only a few sites had implemented the protocol—largely because of competing priorities within their institutions and NCCCP network responsibilities. The continued adoption and implementation of the NCCCP Special Request Biospecimen Disposal SOP is a work in progress. The 2007 pilot sites, and the new sites added to the network in 2010, are increasing the use of policies that incorporate cultural considerations related to the donation of biospecimens.

When developing a similar biospecimen disposal SOP, NCCCP sites suggest that community cancer centers be very mindful of the different cultures they serve. Protocols need to be culturally appropriate and sensitive to the needs of *all* patients.

Case Example—NCCCP Site Billings Clinic

Billings Clinic Laboratory Services at Billings Clinic in Montana has had a biospecimens disposal policy in place since the 1990s. Given the community's significant American Indian population—approximately 6 percent of the regional population—the policy was designed with cultural awareness in mind. Seven reservations are in the Billings Clinic Cancer Center service area. Cancer rates for local American Indians are significantly higher than those for the non-Native American Indians and the survival rates are lower for most cancer types.

Part of the American Indian spiritual belief is to be buried as a whole, creating the need for special disposal requests for tissue or body part collections. Obstacles may be encountered, for example, if there is not notification of the patient's special request before or at the time of surgery, or the laboratory is not aware of the patient's request and the specimen may be disposed of. Communication between the patient, the surgery team, and the pathology department is vital; all three play a critical role in policy adherence. Another unique challenge is that the special request for biospecimen disposal is a paper-based process and, under Montana law, funeral homes are not always directly involved and there is the potential for a communication breakdown.

The Billings Clinic disposal policy was designed for quality patient care and service to ensure respect for the wishes of all patients served at the Clinic. Billings Clinic recognized the importance of developing a policy that was culturally appropriate for the facility's American Indian population. Overall, implementing a disposal policy at Billings Clinic improved cultural awareness for hospital and cancer program staff. Patients, surgeons, surgery staff, pathologists, and pathology staff were all instrumental in the successful implementation of this policy. The Billings Clinic disposal policy served as the starting template for NCCCP sites during the creation of the Special Request Biospecimen Disposal SOP.

Biospecimen Disposal Standard Operating Model Protocol for Special Requests Outside the Scope of Routine Biospecimen Disposal Policy

DRAFT Version 1.3 11.2.09

Purpose:

This model protocol defines a model for the release, at the patient's, or patient's legal representative's request, of any patient biospecimen** that is not subject to local, state, or federal regulations, e.g., bullets, pacemakers, implants, especially in regard to religious, cultural, or other requests. The biospecimen(s) will be released after the pathology evaluation has been completed. *Some of these biospecimens may be bio-hazardous and potentially infectious necessitating decontamination when appropriate and explanation of potential risks to the recipient*.

The facility may wish to include a procedure for re-acquiring the biospecimen if future studies are desirable, e.g., paraffin block. See the College of American Pathologists viewpoint concerning the issue of pathologist legal risk when no diagnostic tissue remains in a paraffin block that is submitted to another laboratory at the patient's request, but is then requested for additional studies by the patient or their physician.

All, portions, or none of this model procedure may be incorporated into the pathology department's policies and procedures at the discretion of the pathology medical director and facility risk management department. This model procedure should not supersede current federal, state, local, or facility regulations.

** Biospecimen is defined as any fluid, cells, tissue, substance, or material removed from the patient for pathology evaluation (clinical and anatomic pathology biospecimens) as well as remnant biospecimen (the biospecimen that is not used during the complete pathology evaluation) and derivative products such as: paraffin blocks, stained and unstained tissue on glass slides, nucleic acids or other derived chemical substances, and digital images.

Procedure:

1. The patient or patient's legal representative must submit a signed request to the pathology department for the release of the specified biospecimen(s). The request form can be filled out before or after collection of the biospecimen and returned to the pathology department with the biospecimen requisition if completed before collection or separately if completed after collection. The Biospecimen Special Disposal Request Form is available from the pathology department (see model form, page 41).

NOTE: As current policy, pathology departments may not release potentially infectious or bio-hazardous biospecimens (e.g., gallbladder stones, gangrenous limb amputations, blood/body fluids, tissue in formalin) to patients, but may release them to legal counsel or mortuaries with appropriate warning and documentation, or to patients after appropriate decontamination (e.g., gallstones that have been rinsed in water and alcohol). Patient viewing and/or provision of photographs of the biospecimen(s) is also used in some pathology departments, thus avoiding release of the biospecimen(s). The potential legal risk for the pathologist if a person becomes infected or injured from a received biospecimen needs to be determined for each facility based on local, state, and federal regulations and precedents.

2. Notification to save the biospecimen is made in writing on the biospecimen requisition form by the collecting or submitting provider if before collection, e.g., physician, nurse, physician assistant, or by the patient or patient's legal representative if after collection and before routine disposal per pathology department policy. The pathology department will hold the requested biospecimen(s) for the patient or patient's legal representative until the appropriate release form has been completed. The patient or patient's legal representative will be notified by phone and by certified letter when the requested biospecimen(s) has completed the final pathology evaluation. A copy of the certified letter and its receipt will be attached to the request form along with a copy of the original biospecimen requisition, all being filed in a confidential and physically secure area. The information and process must be compliant with HIPAA regulations.

3. The biospecimen(s) will be packaged to prevent leakage in case of breakage of a liquid or "in formalin" biospecimen and the package clearly labeled BIO-HAZARDOUS. The patient or patient's representative will complete the release form (Attachment #3): date of pick up, patient's printed name and signature, full contact information of the person picking up the biospecimen such as the current address and phone number, and a witness' printed name and signature that the specimen was received by the stated patient or patient's legal representative (identification must be reviewed) and that biospecimen custodianship has been transferred from the institution to the patient or patient's legal representative.

Frequently Asked Questions:

_____
_____
_____
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_____

Brief synopsis of pertinent policy points:

_____
_____
_____
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_____

Model Biospecimen Special Disposal Request Form
Ver 1.0 9/28/09

Patient's name (printed): _____
Date of biospecimen collection: _____
Biospecimen pathology acquisition number: _____
Biospecimen type to be released: (e.g., blood, tissue, paraffin block, glass slides)
_____

I, (the patient or legal representative), request the release of the above identified biospecimen to me or my legal representative:
Name (printed): _____
Current address (printed): _____
_____
_____
Current telephone number (include area code): _____

I, (the patient or legal representative), understand that the biospecimen I am requesting *may be bio-hazardous and potentially infectious*.
I hereby waive and release (facility name) and its employees and agents from any and all liabilities related to the transfer, handling, and disposition of this biospecimen once it has been released to me or my legal representative.

_____
Printed name of patient or legal representative Date

_____
Signature of patient or legal representative Date

If signed by a legal representative, what is your relationship to the patient? _____

RETAIN A COPY IN THE PATIENT'S FILE AND WITH THE BIOSPECIMEN RESULT REPORT IN THE PATHOLOGY DEPARTMENT.
NCCCP/BS Disposal Project/Model Biospecimen Release Form Ver 1.0 9.28.09

Model Biospecimen Special Disposal Release Form
Ver 1.0 9/28/09

Patient's name (printed): _____
Date of release: _____
Biospecimen pathology acquisition number: _____
Biospecimen type to be released: (e.g., blood, tissue, paraffin block, glass slides)
_____
(Facility name) will release the above identified biospecimen to the following patient or legal representative:
Name (printed): _____
Current address (printed): _____
_____
_____
Current telephone number (include area code): _____

I, (the patient or legal representative), understand that this biospecimen I am receiving *may be bio-hazardous and potentially infectious*. I understand that (facility name) is willing to dispose of the biospecimen, but at my request, has agreed to release the biospecimen to me or my legal representative.

I hereby waive and release (facility name) and its employees and agents from any and all liabilities related to the transfer, handling, and disposition of this biospecimen once it has been released to me or my legal representative.

_____
Printed name of patient or legal representative Date

_____
Signature of patient or legal representative Date

If signed by a legal representative, what is your relationship to the patient? _____

_____
(Name of facility) Representative/Witness (printed and signature) Date

RETAIN A COPY IN THE PATIENT'S FILE AND WITH THE BIOSPECIMEN RESULT REPORT IN THE PATHOLOGY DEPARTMENT.
NCCCP/BS Disposal Project/Model Biospecimen Release Form Ver 1.0 9.28.09

Biospecimen Collection for Molecular Research

One of the goals of the NCCCP pilot was to explore the potential of community hospitals to collect high-quality biospecimens in support of molecular research. It is through the collection of high-quality biospecimens that researchers will be better able to define tumors by genomic and proteomic analyses and develop targeted therapies that are more effective and have fewer toxicities.

Each NCCCP site was encouraged to participate in the collection of biospecimens for molecular research, yet participation was not a requirement. The only subcontract deliverable was the Gap and Fill Assessment Tool (GAFAT), which was used by each site as an indicator of the starting point for each site; the GAFAT measured individual progress and followed the overall progress in building this capacity within the NCCCP network. While each site had its own unique situations and experiences, they were all tasked with assessing their biospecimen collection and storage capacity based on *NCI Best Practices.* The creation of a network of sites that could follow these standards would theoretically create a large source of high-quality biospecimens that were collected, processed, stored, annotated, retrieved, and disseminated in a standardized manner. Adherence to *NCI Best Practices* ensures consistency and harmonization for all resources.

Program Objective and Development

The NCCCP pilot sites evaluated their biospecimen programs and implementation of *NCI Best Practices* using the GAFAT (see page 32). The objective: to improve the quality of biospecimens and/or the biospecimen repository at each NCCCP site.

The consent process is discussed with a Native American patient at Billings Clinic, Montana

Implementation and development of biospecimen collection processes and repositories varied across the NCCCP pilot sites. Three sites (Christiana Hospital, CHI-Penrose, and CHI-St. Joseph/Towson) were selected via a competitive process to participate in The Cancer Genome Atlas (TCGA) after their second year in the NCCCP program. TCGA leadership specifically targeted the NCCCP community hospitals as potential tissue collection sites given their experience in the NCCCP network, noting their attention to the *NCI Best Practices* and their understanding of cancer research's need for high-quality biospecimens. Involvement in the NCCCP prepared the pilot sites for the next stage in the development of their collection processes and repositories. The benefits of TCGA participation included opportunities for the sites to upgrade their tissue procurement databases to caTissue, caBIG®'s biobanking management system, and to strengthen their translational cancer research tissue procurement processes.

Four of the NCCCP pilot sites (Ascension Health–St. Vincent Indianapolis Hospital, Hartford Hospital, Our Lady of the Lake Regional Medical Center, and St. Joseph Hospital/Candler) became associated with Moffitt Total Cancer Care™, which provided staff and financial support to collect high-quality biospecimens; thereby, creating and enhancing development of the sites' biospecimen repositories.

Two sites (St. Joseph Hospital of Orange and Billings Clinic) proceeded with self-initiated, site-specific endeavors, aided by external expertise and mentorship provided by mature NCCCP sites, such as Christiana Care and the CHI (Catholic Health Initiatives) sites. The networking and shared best practices among sites exemplified the power of the NCCCP network and the potential for standardizing processes within the community setting. Funding for the biospecimen repository at St. Joseph Hospital of Orange was secured through fundraising efforts by the institution, bolstered by a $100,000 donation from a local family affected by cancer.

One of the major factors of biospecimen repository success among the pilot sites was the cooperation of surgeons, medical oncologists, pathologists, laboratory staff, research staff, and administration. Cooperation and buy-in from these key stakeholders were essential for the promotion and support of the biospecimen repository within a cancer center and throughout the hospital. Ongoing education at weekly tumor boards also served as a vehicle for identification of patients eligible for tissue procurement.

Educational Opportunities

Presentations by external experts to members of the NCCCP Biospecimens Subcommittee served as valuable educational tools to enhance the biorepository programs at NCCCP sites. Given the spectrum of practice and knowledge among participating institutions, as well as the different backgrounds of individual participants (e.g., pathologists, technologists, and administrators), these discussions helped disseminate information and knowledge to ensure that all network sites had a fundamental grasp of important issues related to the biospecimen repository program.

Speakers covered a broad range of topics, including proper specimen handling and procedures to ensure valid diagnostic testing, the science behind those procedures, as well as more basic research discussions. The role of the NCCCP network was critical to the success of these programs. Without the NCI contacts and the cooperation of the participating institutions, the presentations would not have occurred. Members of the Biospecimens Subcommittee helped to stimulate the presentations by asking questions and guiding discussions to improve audience understanding of the topics. These educational efforts offered potential guidance for NCCCP sites as they developed practices and implemented processes at their respective institutions.

The best presentations were both informative and provided validation for current practices in a particular institution, or offered an outside expert's guidance and rationale to garner institutional support for implementation of a desired best practice. When the NCCCP pilot expansion occurred in 2010, the Biospecimens Subcommittee agreed to solicit feedback from the pilot sites to identify beneficial presentation topics for the new NCCCP sites. The subcommittee also relied on NCI leadership to suggest presentation subjects that would help inform the community cancer centers about early research in progress. The main barrier to success for these educational opportunities was ensuring participation of the appropriate staff. At times, pathologists were unable to participate due to clinical responsibilities, and lack of participation by others (e.g., administrators) led to a lost opportunity to educate and garner institutional support for a change. This obstacle was handled differently by each site. The Biospecimens Subcommittee learned that it was helpful to provide advance information about the presentation topic so that sites could identify the target audience and adjust schedules; they also made presentation material available on the NCCCP's intranet.

Program Challenges

As the pilot sites worked to develop and implement a biospecimen repository program, they reported challenges related to:

- Achieving full cooperation of the pathology department in terms of understanding the scope of the NCCCP program

- Funding and staffing for program support
- IT support from within the cancer center and NCI.

Many NCCCP sites identified pathology support and participation as a necessity, which had to be addressed at the outset of the program. While a few sites reported that funding for program support created challenges, several sites were funded by philanthropic efforts, grants, or outside sources such as TCGA and Moffitt. IT support is an integral part of the biospecimen process, and software applications such as the various caBIG tools (e.g., caTissue) can be costly and difficult to apply to a community-based program without a competent IT staff.

Other challenges included:

- IT infrastructure, implementation, and training
- Standardization of data collection
- Communication—at all levels of hospital organization
- Patient consent—legal, acquisition of consent, patient education
- IRB approval in a timely manner
- Changes required to existing procedures and practices
- Time commitment for participation in the NCCCP.

Program Outcomes

NCCCP sites were recognized locally and nationally for developing biospecimen programs; participation in a network supporting genomic research was an important factor in program progress. The biospecimen programs at several sites allowed patients to participate in clinical trials; led to expanded translational research and participation in programs such as TCGA; and helped increase accuracy and transparency in tracking of lab metrics and sharing of critical data.

Implementation of the formalin fixation best practices for breast specimens (see page 34) was the major accomplishment listed by all NCCCP sites. By 2010 at least one pilot site had implemented formalin fixation best practices for all cancer cases. Sites implementing these processes are prepared to meet the new ASCO/CAP guidelines.[1,2]

The sites identified general benefits of developing and implementing a biospecimen repository, including:

- Access to shared knowledge and experience
- Enhanced program performance due to adoption of the *NCI Best Practices*
- Access to experts and other resources
- Promotion of compliance with formalin fixation guidelines
- New perspectives and increased understanding of biospecimens from an individual and patient perspective to a national and scientific community perspective.

The three-year NCCCP pilot presented educational and networking opportunities and created major changes across NCCCP sites. While several sites entered the early stages of developing and implementing a biospecimen repository, others were able to develop working and contributing biospecimen repositories. Now, all NCCCP sites are using the 2010 *NCI Best Practices* as applicable to their institutions, including processes for consenting, annotating, collecting, processing, storing, and disseminating tissue. These protocols are being used for molecular research and are either already, or will be shortly, used for patient care.

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