Specimen Provenance Complications in the Biopsy Evaluation Process

*Frequency of Occurrence, Detection Methods, and Prevention*

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DIAGNOSTIC ID, LLC
5770 Decatur Blvd
Indianapolis, IN 46241
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I. Background

There are approximately 11.3 million new cancer cases diagnosed annually worldwide which translates to an estimated 38 million biopsy procedures. The U.S. represents approximately 14.5% of the world’s total cancer incidence (1.4 million new cases and 4.8 million biopsies)\(^1\) The process of collecting, handling, analyzing, diagnosing, reporting, and acting upon routine tissue biopsies is complex and involves many steps in the “tissue biopsy → diagnosis → report test” cycle (“Test Cycle”). Despite the utilization of precise labeling systems, the opportunity for diagnostic mistakes due to occult specimen provenance complications persists.

A recent report from the Cleveland Clinic acknowledges the potential for complications is ever-present. The article published by Cleveland Clinic’s Dr. Mary Bronner, M.D., Section Head, Morphologic Molecular Pathology in the Department of Anatomic Pathology states (note: numbers have been added by the author):

“Considering the numerous medical professionals involved in processing a tissue sample from the patient to the pathologist reviewing it microscopically, it is truly a marvel that so few errors occur. Consider that from the patient, a biopsy sample or surgical resection specimen is initially (1) handled by the treating physician using carefully cleaned biopsy and surgical tools that have been used previously to obtain many other patients’ samples. One or more nurses or other assistants assist the physician in (2) getting the tissue sample into a properly labeled specimen container. The specimen container is (3) batched with many other containers and (4) transported to the pathology laboratory. There, the specimen is (5) accessioned into the pathology computer system and is (6) assigned a unique surgical pathology identifier. Next, the paperwork and specimen container are (7) processed by a pathology assistant, resident, or pathologist who removes the specimen from the labeled container and examines and describes the tissue grossly. The tissue is (8) dissected by carefully cleaned instruments that also are used to dissect many other patients’ samples. The specimen is (9) divided among a number of tissue cassettes, small plastic containers, which are (10) labeled individually with the surgical pathology number and a unique block number. The tissue cassettes have holes in them to permit flow of the various processing fluids required to process the tissue chemically into a final wax tissue block. Many hundreds of different patients’ cassettes are (11) placed into a common chemical bath for this processing stage. Rarely, a tissue fragment from one patient can exit its cassette and enter through the

\(^1\) American Cancer Society, Cancer Facts and Figures 2008 and 2002 Study by the Agency For Research on Cancer
cassette holes of another patient’s block to become part of this second patient's block. A histotechnologist uses clean forceps, which are cleaned and used subsequently on many other patients’ specimens, to (12) pick up the wax-infused tissue fragments from the processing cassettes and place them into the final wax tissue block that will be used to section the actual histologic slides. Another histotechnologist (13) sections 5 µm slices on a razor blade affixed to a microtome. These thin wax slices are (14) floated onto a carefully cleaned water bath, which has had many other patients’ wax slices previously floating in it. Floating allows slices to flatten and be (15) transferred onto a glass slide, which has been hand-labeled by the histotechnologist. The slide later receives a permanent computer-generated slide label that is (16) affixed to the slide by another technician. Finally, all of the slides on any given patient’s procedure are (17) assembled with the accompanying paperwork and (18) delivered to the pathologist for diagnostic interpretation. A mistake leading to inadvertent tissue contamination can occur at any one of the above logistically complex processes.2

THE IMPORTANCE OF ESTABLISHING SPECIMEN PROVENANCE

Due to the scale and complexity of the biopsy evaluation process described above, combined with the critical importance of diagnostic accuracy, it is essential to develop objective means of establishing specimen provenance. For the purposes of this paper “specimen provenance” is defined as having certainty that a histopathology tissue under examination derives exclusively from a specific identified patient.

Failure to establish specimen provenance introduces an opportunity for misdiagnosis. These instances - called Specimen Provenance Complications (SPC) - jeopardize patient safety and diagnostic accuracy and can lead to adverse patient outcomes (ie. overtreatment / undertreatment). SPCs are an inherent byproduct of the complex biopsy evaluation process and may result from instances of specimen transposition, foreign cell contamination, and patient misidentification occurring in clinical or anatomical pathology.

Appendix A of this paper features summaries of research that examine some root causes of Specimen Provenance Complications.

Appendix B of this paper details cases that demonstrate the consequences of Specimen Provenance Complications.

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2 Bronner. DNA Fingerprint Analysis for Specimen Identification. Cleveland Clinic Clinical and Translational Pathology Research. 2006; Fall: 5-7.
II. Specimen Provenance Complications Are Not Uncommon

“Misidentification errors are common in laboratory medicine…” according to the College of American Pathologists, whose extrapolation of reported errors from 120 recently studied pathology laboratories indicates that at least 2.9 million laboratory specimen misidentifications lead to more than 160,000 adverse patient events per year in the U.S.\(^3\).

And according to a study of switching errors performed at the Baptist Hospital of Miami in Miami, Florida during 2005 and 2006, “……because of the relatively high number of cases received by this laboratory, this problem [switching of biopsies] occurs several times each year.”\(^4\)

A Wall Street Journal article from June 2006 reports, “3 percent to 5 percent of the billions of specimens taken each year are defective be it a biopsy that doesn't extract the tumor cells, blood that isn't drawn correctly or a mix-up with another patient's sample.”\(^5\)

It is difficult to know the extent of specimen provenance complications since many instances remain occult, that is, one cannot “know” what is “unknown”. And of those that are detected, those which are reported may be merely a small subset of all instances (\textit{refer to diagram 1}). As such, estimates of SPCs calculated from that which is reported must surely underestimate the total number of SPC instances. A College of American Pathologists study cautions that the \textit{true incidence of both errors AND resulting adverse events is much higher than can be presently...}
measured. This is especially important since SPCs are created along the entire test cycle, regardless of the specific setting for the pre analytic, analytic, and post analytic steps for a particular patient specimen.

III. Reducing Errors: An Initial Step in Minimizing Specimen Provenance Complications

Based on the studies referenced in the previous section (and others like them) a number of systems (i.e. quality improvements) have been suggested and/or utilized in an effort to reduce the number of errors that lead to SPC. These include:

**Bar Coding**
Probably the most common identification error reduction strategy in laboratory use today is simply to replace or supplement hand written identification with computer generated and computer read bar-codes. Though still not nearly as pervasive in laboratory settings as other industrial, retailing, and logistics arenas, bar-coding is a very cost effective means of tracking specimens and applying a degree of scientific precision to identification not possible from manual methods. Bar-codes are dramatically less susceptible to human error than any form of hand-written and visually interpreted identification.

**Inking**
One such error reduction method is the “inking” of specimens whereby at the time of grossing, each specimen is directly inked through the bag in one of 6 colors. The colors are always applied in the same sequence. The dissector writes the color used on the original requisition slip and dictates the color for the gross description. Each block is then routinely processed and entirely sectioned to produce at least 5 slides and 2 levels per slide. When the slides from the cases are reviewed, the pathologist compares the color of the ink in the tissue with that written in the gross description.

**RFID**
Yet another error reduction method is suggested by the Mayo Clinic. Mindful of their lab’s number of identity errors and the potential for

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7 Andrew A. Renshaw, MD, Richard Kish, MHS, and Edwin W. Gould, MD The Value of Inking Breast Cores to Reduce Specimen Mix-up

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adverse consequences, the Mayo Clinic recently adopted radio frequency technology in their GI lab in Rochester MN in an effort to determine and the reduce the incidents of identification errors.

MAYO CLINIC STUDIES GI SUITE LABELING ERRORS

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http://www.endonurse.com/
Posted on: 10/07/2008

ROCHESTER, Minn. — Mayo Clinic researchers are recommending a new technologically-advanced labeling system aimed at reducing specimen labeling errors in high-volume gastrointestinal endoscopy centers. “The gastroenterology and colorectal surgery outpatient endoscopy unit at our facility yields over 30,000 specimen bottles that are sent for pathologic review every year,” said Dawn Francis, MD, the lead author and a gastroenterologist at Mayo Clinic. "Over the past several years, Mayo Clinic identified some issues with mislabeling of tissue specimens in the units. Most labeling errors have been due to either the wrong patient label or no label being affixed to a specimen bottle. As a result, a quality improvement initiative was created to reduce the number of specimen-labeling errors."

This study used a technology, radio-frequency identification (RFID), to track biopsy specimens taken during gastrointestinal endoscopic procedures and to automate identification. An RFID tag can be applied to or incorporated into an object so that it can be identified by using radio waves. Radio-frequency identification is used in other settings, such as libraries or passports, as an automated tracking system. This is its first application to track specimens in a healthcare setting. Researchers reviewed the number of specimen-labeling errors for the first three months of 2007, prior to the implementation of the initiative and the first three months of 2008, six months after the initiation of RFID specimen labeling. Specimen-labeling errors were categorized as Class 1 (only typographical with no potential patient care consequences), Class 2 (minor error, unlikely to have patient care consequences) and Class 3 (significant error that has the potential to detrimentally impact patient care).

The endoscopy unit sent 8,231 specimen bottles to the pathology laboratory for evaluation during the first three months of 2007, and 8,539 bottles in the first three months of 2008. Compared to 765 errors in 2007, only 47 errors were noted in 2008. Overall, serious errors were low anyway, but the new labeling system reduced such errors even more, minimizing risk for patients. The two incidents of Class 3 errors in the first quarter of 2008 were recognized and corrected prior to specimen processing in the pathology laboratory." This system has provided us a great opportunity to enhance safety and quality efforts in specimen management. The RFID system has
allowed us to reduce the number of data transcription points during the handling of these very important specimens," said Schuyler Sanderson, MD, a pathologist involved in the research study. "It appears that this quality initiative, with emphasis on correct data creation and transcription point reduction, has the potential to significantly improve our clinical practice."

Previous Mayo Clinic research on RFID technology revealed that human error decreased dramatically as multiple checkpoints in specimen handling were eliminated.

Note that per the Mayo clinic study referenced above, in Q1 of 2008 AFTER implementing an error reduction program (i.e. state of the art RFID), 47 errors were still made! The errors with which Mayo reported were only those that were detected (i.e. known), a subset of the actual number of errors (see Diagram 1). Since errors still can occur even after implementation of an "error reduction system", patients remain exposed to the risk of overtreatment/undertreatment, and the hospital/physician reputation remains at risk.

Although systems such as those mentioned above have the effect of reducing errors of specimen provenance, there is still a possibility that some instances will remain undetected. Therefore a system to establish specimen provenance (and thus prevent adverse patient outcomes) seems to be very desirable.

IV. A Method to Establish Specimen Provenance

(both previously known, and unknown errors) i.e. to “know” what is not “known”

The use of forensic DNA to identify unknown tissues and matching to a reference sample is one method by which specimen provenance can be established.

DNA “fingerprinting” analysis by polymerase chain reaction (PCR) is a highly accurate technique for determining patient identity for a tissue sample. This test is used in forensic pathology for criminal identification and can be useful in surgical and autopsy pathology when the patient identity of tissue samples is in question.

In the Journal Of Urology (October 2007), Drs. John Pfeifer, Stephen Raab, and Eric Suba suggested that the medical community may be ready for a “DNA Timeout” utilizing forensic DNA, an abstract of which follows:

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**PATIENT IDENTIFICATION ERROR AMONG PROSTATE NEEDLE CORE BIOPSY SPECIMENS: ARE WE READY FOR A DNA TIME-OUT?**

**Eric J. Suba, John D. Pfeifer and Stephen S. Raab**
From the Kaiser Permanente Medical Center (EJS), South San Francisco, California, Washington University Medical Center (JDP), Saint Louis, Missouri and University of Pittsburgh Medical Center (SSR), Pittsburgh, Pennsylvania

**Purpose:** Patient identification errors in surgical pathology often involve switches of prostate or breast needle core biopsy specimens among patients. We assessed strategies for decreasing the occurrence of these uncommon and yet potentially catastrophic events.

**Materials and Methods:** Root cause analyses were performed following 3 cases of patient identification error involving prostate needle core biopsy specimens.

**Results:** Patient identification errors in surgical pathology result from slips and lapses of automatic human action that may occur at numerous steps during pre-laboratory, laboratory and post-laboratory work flow processes.

**Conclusions:** Patient identification errors among prostate needle biopsies may be difficult to entirely prevent through the optimization of work flow processes. A DNA time-out, whereby DNA polymorphic microsatellite analysis is used to confirm patient identification before radiation therapy or radical surgery, may eliminate patient identification errors among needle biopsies.

**DNA FINGERPRINTING**

Another advocate of so-called DNA fingerprinting is Mary P. Bronner, M.D of the Cleveland Clinic. Highlights from her article are outlined below.

**Background**
DNA fingerprinting analysis by polymerase chain reaction (PCR) is a highly accurate technique for determining patient identity for a tissue sample. This same test is used in forensic pathology for criminal identification, but it is equally useful in surgical and autopsy pathology when the patient identity of tissue samples is in question.

**Clinical Indications**
Assessment of tissue identity by DNA fingerprinting is useful for confirming possible tissue contaminants identified on histological slides and for determining specimen identity in the case of suspected mislabeling or unlabeled samples. A common example of such testing regards the finding of a cancer fragment on a patient’s slide when no cancer is suspected clinically. A specific example would be a fragment of cancer that appears on an otherwise normal 12 year-old child’s benign appendectomy specimen.

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9 Bronner. DNA Fingerprint Analysis for Specimen Identification.Cleveland Clinic Clinical and Translational Pathology Research. 2006; Fall: 5-7.
Initially, the pathologist determines whether the cancer fragment is on only one profile of the multiple slices of tissue on the slide, in which case it is easily dismissed as a so-called “floater” or fragment left behind in an improperly cleaned water bath used to prepare slides. In the event that the cancer fragment is on all of the different slices from a given tissue block, DNA fingerprinting can be used to determine whether it belongs to this hypothetical 12 year-old patient undergoing appendectomy. If the DNA from the cancer fragment differs from the benign appendix tissue on the slide, the cancer fragment is an inadvertent contaminant. The certainty involved in knowing that a given patient does not have cancer is of obvious and great importance.

Another article follows suggesting the use of DNA to ensure biopsy material is correctly identified.10

SORTING OUT MIX-UPS. THE PROVENANCE OF TISSUE SECTIONS MAY BE CONFIRMED BY PCR USING MICROSATELLITE MARKERS

O’Brian DS, Sheils O, McElwaine S, McCann SR, Lawler M.

Abstract
Standard identification systems usually ensure that biopsy material is correctly associated with a given patient. Sometimes, as when a tumor is unexpectedly found, the provenance (proof of origin) of a tissue sample may be questioned; the tissue may have been mislabeled or contaminated with tissue from another patient. Techniques used to confirm tissue provenance include comparing either tissue markers of gender or ABO blood groups; however, these methods have weak confirmatory power. Recently, the use of DNA-based polymerase chain reaction (PCR) techniques has been reported. Paired, formalin-fixed, paraffin-embedded, 10 microns tissue sections were selected from 17 patients, 8 of whom had carcinoma, either by dividing a biopsy section, using sequential biopsies, or sequential biopsy and autopsy tissue. The resulting 36 samples were coded before analysis. In two additional cases, 1-mm fragments of tumor from one patient were included in the tissue block of benign tissue from another patient, the tumor fragments were identified on hematoxylin-and-eosin-stained sections, separately scraped off the glass slide, and analyzed. Tissue from two clinical cases, one of suspected mislabeling and

10 American Journal of Clinical Pathology 1996 Dec; 10696):758-764
one with a suspected carry-over of malignant tissue were also investigated. Short tandem repeat sequences (STR) or microsatellites, are 2-5 base pair repeats that vary in their repeat number between individuals. This variation (polymorphism) can be assessed using a PCR. A panel of markers of 3 STRs; ACPP, INT 2, and CYP 19 (on chromosomes 3, 11, and 15, respectively) were used. DNA was isolated from the samples after xylene deparaffinization and proteinase digestion, and was then amplified in a radioactive PCR using primers selected to give a product size ranging from 136-178 bases. Amplified products were electrophoresed on denaturing polyacrylamide gels, dried, and autoradiographed. DNA segments were successfully extracted from all samples but one, which was fixed in Bouin's fluid. By comparing allele sizes from the panel, all tissue pairs (other than the Bouin's pair) were successfully matched, the 1-mm tumor fragments were correctly assigned, and the two clinical problems were solved. STRs are highly informative and robust markers, well suited to PCR of small portions of tissue sections, and are an effective method to confirm the provenance of benign and malignant biopsy and autopsy material.

V. Method to Prevent Adverse Patient Outcomes Due to Specimen Provenance Complications

As identified in this paper, DNA “fingerprinting” has been advocated to establish specimen provenance even among those systems which adopt precise error reduction programs (e.g. RFID or bar-coding). This DNA testing, known by various names, is offered by Mayo Clinic, Cleveland Clinic, Johns Hopkins and the Indiana University Medical Center, for example. For the purposes of this paper, we shall refer to this test as DNA Specimen Provenance Assay (DSPA).

The utilization of DSPA PRIOR TO INITIATING TREATMENT is a method to prevent adverse patient outcomes (i.e. overtreatment / undertreatment) due to Specimen Provenance Complications. Only by developing a DNA profile from a reference sample from a patient and matching it to the DNA profile from a tissue sample from the patient can a physician be certain that the tissue is that of the patient. And only by performing DSPA matching prior to the initialization of treatment can patient safety be assured and quality of care improved. Performing such a test post-treatment does not increase patient safety.
THE KNOW ERROR® SYSTEM

One system that incorporates both error reduction measures AND DSPA is the KNOW ERROR® system developed by Diagnostic ID, LLC. The know error® system employs both bar-coding AND DSPA confirmation in a prospective process which, when adopted by pathology labs and their referring physicians, establishes specimen provenance, and, in so doing, eliminates any adverse patient outcomes due to SPCs.

HOW THE KNOW ERROR® SYSTEM WORKS

Tagging: The know error® system biopsy kits employ patient specific ID codes or “tags” in the form of two-dimensional bar-codes. Each kit is assigned a unique bar-code number (both human and computer readable), and every individual component of the kit is tagged with the matching code -- the benefit of which is a system for consistent patient identification and a reduction of errors.

DSPA Testing: Included in the know error® system kits are cotton swabs (“buccal swabs”) used to obtain a DNA reference sample from the patient by swabbing the inside of his or her cheek. This is the very first step in the know error® system’s biopsy protocol, and establishes the initial link between the patient and the assigned kit’s unique number – at both an administrative and molecular level. After self-identification by the patient, the buccal swabs are sent directly to a forensic DNA lab where they are accessioned and stored. Once a comparison with pathology tissue is ordered by the physician, the biopsy tissue used by the pathologist for diagnosis is sent to the forensic DNA lab whereby DNA is extracted and then compared with DNA extracted from the buccal swab having the identical bar-code tag. A DSPA report is issued within 5 business days of receipt of the tissue indicating whether or not specimen provenance has been established.

DSPA tests are performed via PCR (polymerase chain reaction) and electrophoresis techniques developed for the forensic identification of biological materials11. Unlike visual inspection of hand-written patient records, tissue slide labels, and pathology reports, forensic DNA matching provides an absolute and unambiguous confirmation of identity. The benefit of DNA

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11 The protocol examines the same 16 genetic loci as those commonly used for forensic identification by the FBI and other international authorities. These loci and techniques represent the international gold-standard for human identification in the forensic community.
matching is establishing specimen provenance, thus, helping to prevent adverse patient outcomes.

EMPIRICAL DATA

An internal report issued by Diagnostic ID regarding the results of twelve months’ worth of data from Diagnostic ID clients is summarized here.

Background
The know error® system is a system for establishing specimen provenance and includes a DNA Specimen Provenance Assay (DSPA). The result of a DSPA test is an integral component of the body of information obtained by the ordering physician to inform his accurate and timely diagnosis of certain cancers. Specifically, DSPA testing prevents misdiagnosis and inappropriate or unnecessary medical treatment which can result from occult specimen provenance complications such as specimen contamination or misidentification. Using microsatellite analysis, the know error® system was implemented in the offices of urologists and pathology labs around the United States from the period May 1, 2009 through October 22, 2010. Patients undergoing a prostate biopsy submitted a reference DNA sample on a buccal swab prior to the prostate biopsy. The bar coded buccal swab was sent directly to a forensic DNA lab. The pathology labs sent all positive specimens to the forensic DNA lab for a DNA Specimen Provenance Assay to confirm a match between the patient’s reference DNA buccal swab and the positive tissue specimen(s).

Results
Between 5/1/09 and 10/22/10, over 17,000 patients underwent prostate biopsies and submitted a reference DNA buccal swab. 5598 patients were diagnosed with prostate cancer and positive biopsy specimens were sent for a DNA Specimen Provenance Assay (DSPA) utilizing microsatellite analysis.

Specimen Provenance Complications identified as a “DNA non-match” were found in 57 patients (1.02%) resulting from specimen switches or mixed specimen contamination. Additionally, over 100 recordkeeping errors were identified during the accessioning process by the forensic DNA lab, many of which, if left uncorrected, might have resulted in a “DNA non-match.” These errors included patient self-identification records not matching the pathology lab’s records (e.g. name mismatch, date-of-birth mismatch).
Impact
Until recently, the intrinsic patient safety issues resulting from SPCs have not been measured thoroughly or studied on a prospective basis, and physicians have had little choice but to accept them as a tolerable component of diagnostic imprecision in the tissue biopsy → diagnosis → report test cycle (“Test Cycle”). However, recent advances in molecular diagnostics techniques enable clinicians to reach a level of diagnostic accuracy from the Test Cycle at a level of sensitivity consistent with national patient safety goals and requirements.

In order to obtain a body of information sufficient to make accurate cancer and other diagnoses, many physicians have adopted a standard of care that mandates two steps to all biopsy procedures: (1) conventional histopathology/microscopy; and (2) DSPA testing. It is the opinion of a growing number of clinicians that, given the patient safety risks inherent in the complex Test Cycle, it is inappropriate to make treatment decisions based on biopsy interpretation unless the histopathology is combined with DSPA testing. This is particularly true when treatment options include radical surgical procedures, radiological and/or chemical therapies, or for disease states where lack of early detection can have a significant negative impact on patient outcomes.

VI. Cost-Effectiveness of DSPA

DSPA testing is highly cost-effective based on preliminary results from a medical economics paper prepared for publication by members of the Center for Health Policy and the Department of Pathology at Washington University School of Medicine in St. Louis, Missouri. Specifically, the paper calculates the cost-effectiveness of DSPA testing done on a prospective basis for patients undergoing a prostate biopsy and concludes that there is “a cost efficiency of testing.”

VII. Summary

The biopsy evaluation process is inherently complex, and establishing specimen provenance is a key component of providing an accurate diagnosis. Mechanisms in place to reduce errors in the biopsy evaluation process remain insufficient and inferior to systems which establish specimen provenance. Ultimately an objective means of establishing provenance –
where cost-effective – is desirable and beneficial to physicians, laboratories and the patients they serve.

CONCLUSION

A cost-effective system (such as the know error® system) used by the medical community which establishes specimen provenance (by means of DSPA) protects patients from adverse outcomes and provides physicians with the confidence to administer appropriate treatment protocols.

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Appendix A: Causes of Specimen Provenance Complications:

PUBLISHED ESTIMATES

Specimen Provenance Complications (SPC) are a consequence of the complex biopsy evaluation process and arise due to instances of specimen transposition, foreign cell contamination, and patient misidentification that occur in clinical and anatomical pathology. Following are some published reports which review possible causes and frequencies.

1) PATIENT IDENTIFICATION IN A CLINICAL LAB:
A College of American Pathologists Q-Probes Study of Patient and Specimen Identification Errors at 120 Institutions.

College of American Pathologists, Valenstein PN, Raab SS, Walsh MK.

Department of Pathology, St Joseph Mercy Hospital, Ann Arbor, Mich 48106-0998, USA. paul@valenstein.org


CONTEXT: Misidentified laboratory specimens may cause patient injury, but their frequency in general laboratory practice is unknown.

OBJECTIVES: To determine (1) the frequency of identification errors detected before and after result verification, (2) the frequency of adverse patient events due to specimen misidentification, and (3) factors associated with lower error rates and better detection of errors.

DESIGN: One hundred twenty clinical laboratories provided information about identification errors during 5 weeks.

RESULTS: In aggregate, 85% of errors were detected before results were released; one quarter of laboratories identified more than 95% of errors before result verification. The overall rate of patient identification errors involving released results was 55 errors per 1,000,000 billable tests. A total of 345 adverse events were reported. Most of the adverse events caused material inconvenience to the patients but did not result in any permanent
harm. On average, adverse events resulted from 1 of every 18 identification errors. Extrapolating the adverse event rate observed in this study to all United States hospital-based laboratories suggests that more than 160,000 adverse events per year result from misidentification of patients' laboratory specimens.

CONCLUSIONS: Identification errors are common in laboratory medicine, but most are detected before results are released, and only a fraction are associated with adverse patient events. Even when taking into consideration the design of this study, which used imperfect case finding, institutions that did a better job of detecting errors within the laboratory released a smaller proportion of results that involved specimen misidentification.

Author’s annotation: Total detected identification error rate...0.03%. The portion not detected prior to release...0.01%. Estimated 161,000 adverse events per year in US result from misidentification of laboratory specimens. The estimates were based on known errors. No estimate was made of the number of undetected errors.

2) SPECIMEN PROVENANCE AND SURGERY PATIENTS:
A New Measure of Quality In Surgical Care

Martin A. Makary, MD, MPH  Jonathan Epstein, MD, Peter J. Pronovost, MD, PhD, E. Anne Millman, MS, Emily C. Hartmann, MS, and Julie A. Freischlag, MD,

BACKGROUND: Communication errors are the primary factor contributing to all types of sentinel events including those involving surgical patients. One type of communication error is mislabeled specimens. The extent to which these errors occur is poorly quantified. We designed a study to measure the incidence and type of specimen identification errors in the surgical patient population.

METHODS: We performed a prospective cohort study that included all patients who underwent surgery in an outpatient clinic or hospital operating room and for whom a pathology specimen was sent to the laboratory. The study took place during a 6-month period (October 2004 to April 2005) at an urban, academic medical center. The study’s main end-points were the incidence and type of specimen labeling errors in the hospital operating room and the outpatient clinic. The specimen was the unit of analysis. All specimens were screened for “identification errors,” which, for the purposes of this study, were defined as any discrepancy between information on the specimen requisition form and the accompanying labeled specimen received in the laboratory. Errors were stratified by the type of identification error, source, location, and type of procedure.

RESULTS: A total of 21,351 surgical specimens were included in the analysis. There were 91 (4.3/1000) surgical specimen identification errors
(18, specimen not labeled; 16, empty container; 16, laterality incorrect; 14, incorrect tissue site; 11, incorrect patient; 9, no patient name; and 7, no tissue site). Identification errors occurred in 0.512% of specimens originating from an outpatient clinic (53/10,354 specimens) and 0.346% of specimens originating from an operating room (38/10,997 specimens). Procedures involving the breast were the most common type to involve an identification error (breast:11, skin:10, colon: 8); in addition, 59.3% (54/91) of errors were associated with a biopsy procedure. Follow-up was complete in all cases found to have an identification error.

CONCLUSIONS: Surgical specimen identification errors are common and pose important risks to all patients. In our study, these events occurred in 4.3 per 1000 surgical specimens or an annualized rate of occurrence of 182 mislabeled specimens per year. Given the frequency with which these errors occur and their potential effect on patients, the rate of surgical specimen identification errors may be an important measure of patient safety. Strategies to reduce the rate of these errors should be a research priority. (Surgery 2007;141:450-5.)

Author’s annotation: Detected patient identification error rate...0.05%. No estimate was made of the number of undetected errors.

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Appendix B: Consequences of Occult Specimen Provenance Complications

Unidentified Specimen Provenance Complications involving specimen switching or contamination can result in misdiagnosis and mismanagement of patients with potentially catastrophic results. Patients may undergo radical surgery, radiation therapy, or chemotherapy for a cancer diagnosis that has been incorrectly assigned to a cancer-free patient. Moreover, the corresponding failure to treat a cancer patient at the earliest possible opportunity may also have undesirable consequences. Adverse patient outcomes also have both medical and legal consequences for every person and/or entity involved in the biopsy process.

FOUR EXAMPLES OF ADVERSE (PATIENT) OUTCOMES DUE TO SPECIMEN PROVENANCE COMPLICATIONS

1) MEDICAL MIX-UP, UNNECESSARY MASTECTOMY
(excerpt) Cancer-Free Woman Underwent Double Mastectomy Because of Lab MixUp
Mike Celizic TODAYShow.com contributor updated 8:46 a.m. ET, Thurs., Oct. 4, 2007

Because of a mislabeled tissue sample that led to a misdiagnosis, Darrie Eason had both of her breasts removed to save her from a cancer that she never had.

No amount of money will make Eason whole again, but the Long Island, N.Y., woman hopes that her experience and a lawsuit she is pressing may help other women. “Maybe if people hear about my case, they’ll know. Maybe somebody will do something differently next time,” she told TODAY co-host Meredith Vieira during an interview Thursday. “I don’t want this to happen to anyone else.” Eason is a 35-year-old single mother who works in the accounts receivable department of a local community newspaper chain. She has a 15-year-old son. In 2006, she was told she needed to undergo a radical double mastectomy because she had an invasive form of breast cancer. “I just broke down and cried,” she recalled of the moment she got the diagnosis. Eason went to another doctor for a second opinion, and was again told she had cancer. The doctor relied on the same mislabeled tissue sample.

“I was told I had lobular breast cancer, which everybody said would come back,” she told Vieira. Armed with that information, she had both breasts
removed and underwent the first phase of reconstructive surgery in May 2006. While waiting to heal so she could begin chemotherapy, her surgeon, who had submitted removed tissue to a lab for routine testing, told her that something was wrong: **She didn’t have cancer.** “You can’t even explain it,” Eason said of her emotions when she was told she had had both her breasts removed for no reason. An investigation by the New York State Department of Health would reveal that the lab that handled her biopsy samples had mixed up her sample with that of another woman.

The other woman, who actually did have breast cancer, was told she was cancer-free. Only when Eason’s error was discovered did the other woman, whose identity has not been revealed, learn that she had cancer. “She has to live with the idea that she had breast cancer and hers was not diagnosed at the earliest possible time,” said Eason’s attorney, Steven Pegalis, of the other woman. The state report said “the most likely source of the error” was the technician engaging in a practice called “batching,” which involves handling more than one specimen at a time. The state health department determined that the lab’s error was isolated and found “no systemic problems and no deficiencies” at the lab. Eason’s attorney, Steven Pegalis, told Vieira he’s not so sure. “It may be one person, but personally I doubt it. One of the things we may learn is ‘Was there a system failure, and if so, what can be done to improve the system?’ Personally, I doubt this is a one-time event by someone who was careless for one time in his or her life,” he said.

### 2) MAN SUES AFTER HE’S WRONGLY DIAGNOSED WITH CANCER; HAS RIGHT BREAST REMOVED

*Thursday, May 14, 2009  NY Daily News AP*

A suburban New York City man is suing a hospital and three doctors for performing a radical mastectomy on him even though he never had cancer. Personal trainer Scott Aprile says that two weeks after the January surgery, one of the doctors told him his biopsy had been switched with another patient’s and he never had cancer.

Nyack Hospital in Rockland County tells the Daily News it “regrets the circumstances leading to the misidentification” and says new preventive measure are in place. The hospital is also calling Aprile’s allegations “inflammatory and factually inaccurate.” The 28-year-old Aprile says he’s still in pain after having his right breast and three lymph nodes removed and doesn’t know if he can go back to work.
3) MOTHER’S HEALTHY OVARIIES REMOVED IN LAB MIX-UP

*Mass Lawyers Weekly*
Published: July 31, 2008
*$315,000 settlement*

On May 27, 2005, a 48-year-old married woman and mother of a young child saw her obstetrician-gynecologist because of abnormal vaginal bleeding. An endometrial biopsy was performed to determine whether the bleeding was cancer-related. She had previously suffered from breast cancer five years earlier and therefore was at risk for metastases.

One week later, she was told that the pathology report indicated she may have cancer. Consequently, on June 9, she underwent a total abdominal hysterectomy and ovary removal. A week after the operation, the surgeon told her that when he looked at her organs during the operation, he had not seen any cancer and that the pathology report from the surgery did not evidence any cancer cells.

When she asked him how the initial pathology report could have shown cancer if the post-operative report was negative, he told her he did not have an answer.

The woman proceeded to investigate on her own. In late July 2005, she sent her slides to the pathology departments at other hospitals to confirm the diagnosis of cancer on the original slides. When they confirmed the results, she pushed for DNA testing to determine whether the original slides showing cancer consisted of tissue from her body. Eventually, on March 9, 2006, she learned that the DNA testing confirmed that her slides had gotten “cross-contaminated” in the lab with those of another woman who had endometrial cancer. **The patient never had endometrial cancer.**

Due to this lab error, she had her entire uterus, cervix and ovaries removed unnecessarily. Following surgery, she was in extreme pain. In addition, the wound did not heal completely, and she had to return to the hospital to have a stitch removed that was protruding through her skin. She was left with a disfiguring bump on her stomach and a six-inch scar. She also went through emotional turmoil throughout the nine months that she believed she had endometrial cancer.

The devastating psychological impact of the mistake was compounded by the fact that she previously had suffered breast cancer. By 2005, she had managed to survive five years post-diagnosis and believed she was cancer-
free. Her greatest concern, that the cancer would someday metastasize, was seemingly realized.

Type of action-Medical malpractice
Injuries alleged-Misdiagnosis and unnecessary operation causing pain, suffering and emotional anguish
Amount of settlement-$315,000
Attorney-Jeffrey N. Catalano, Todd & Weld, Boston (for the plaintiff)
Date of Verdict or Settlement-04-Aug-08

4) TWO MEN FILE LAWSUITS OVER PROSTATE BIOPSY MIX-UP

*The Boston Globe*
Published: August 2, 2010

Two male prostate biopsy patients in the Boston area suffered adverse outcomes due to Specimen Provenance Complications.

The first patient – Manuel Barros – underwent radical prostatectomy surgery only to discover after the fact he did not actually have cancer. The pathologist who analyzed his biopsy in November had mistaken his slides for those of another patient who did have prostate cancer, according to a report Beth Israel filed with the state. As a result of the unnecessary surgery, Barros now suffers from erectile dysfunction and incontinence.

The second patient – Thomas Cloutman – was initially told he was cancer free, but it was later discovered eight months later that his sample was mixed up at the lab. Mr. Cloutman had surgery to remove his prostate in January at Boston Medical Center, he said, but doctors found that cancer had spread to a lymph node. Now he is weighing the possibility of radiation therapy.