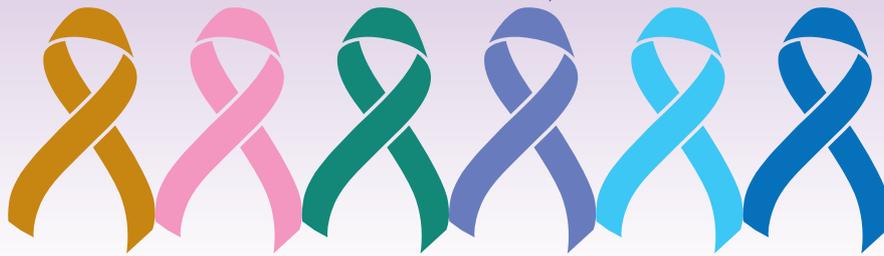


MINISTRY OF HEALTH



NATIONAL CANCER SPECIMEN HANDLING GUIDELINES

2020





MINISTRY OF HEALTH

National Cancer Specimen Handling Guidelines

Developed by the National Cancer Control Program, Department of Non-Communicable Diseases
Ministry of Health

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Abbreviations and acronyms

BMA	Bone Marrow Aspirate	MDT	Multidisciplinary Tumor Board
BMT	Bone Marrow Trephine	ME	Margin Evaluation
BRCA	Breast Cancer gene	MOH	Ministry of Health
CIN	Cervical intraepithelial neoplasia	MRM	Modified radical Mastectomy
CIS	Carcinoma in Situ	MTRH	Moi Teaching and Referral Hospital
CQI	Continuous quality Improvement	NCCP	National Cancer Control Program
DHIS	District Health Information System	NPHLS	National Public Health Laboratory Services
DNA	Deoxyribonucleic Acid	PET	Positron Emission Tomography
EQA	External Quality Assurance	PPE	Personal Protective Equipment
ER	Oestrogen receptor	PSA	Prostate specific Antigen
EUA	Examination under Anaesthesia	QA	Quality Assurance
FFPE	Formalin Fixed Paraffin Embedded	SOPs	Standard Operating Procedures
FNA	Fine Needle Aspirate	TAT	Turnaround time
HER2	Human epidermal receptor2	TURP	Trans urethral resection prostate
HGD	High Grade Dysplasia	UHC	Universal Health Coverage
HNPCC	Hereditary non polyposis colon cancer	VIA	Visual Inspection with acetic Acid
HPV	Human Papilloma virus	VILI	Visual Inspection with Lugo's iodine
HSIL	High grade Squamous Intraepithelial Lesion	WHO	World Health Organization
IARC	International Agency for Research in Cancer		
IATA	International Air Transport Association		
IQA	Internal Quality Assurance		
IQC	Internal Quality Control		
KMLTTB	Kenya Medical Laboratory Technologist and Technician Board		
KNH	Kenyatta National Hospital		
LMIS	Laboratory Management Information System		
LMIC	Low middle income countries		



Foreword

The right to health is a fundamental human right guaranteed in Article 43 1 (a) of the constitution of Kenya. The Kenya Cancer Policy 2019-2030 aims to promote access to optimal cancer diagnostics and treatment.

Diagnosis is the entry point to cancer care. The National Cancer Specimen Handling Guidelines 2020 have been developed in line with the implementation of Pillar 2 (Diagnosis, Registration and Surveillance) of the National Cancer Control Strategy 2017-2022. Approximately 70-80% of all cancer patients in Kenya are diagnosed at advanced stages of the disease when it is not amenable to optimal treatment leading to poor treatment outcomes and high mortality rates. Some of the contributing factors to late diagnosis include delayed, incomplete or inaccurate diagnosis as well as sub-optimal handling of cancer specimens leading to long turnaround times before a definitive diagnosis is made. Poorly handled cancer specimens also contribute to potential loss of critical pathological data leading to unsuitability for advanced tests such as immunohistochemistry which provide additional information to guide treatment decisions.

The purpose of these guidelines is to standardize and optimize cancer diagnosis for priority cancers through proper handling, processing of specimens and referrals. They emphasize gold standard pathology reporting protocols and prescribe the minimum clinical and pathological datasets for common cancers in Kenya in accordance with current evidence and international best practices.

It is my hope that these guidelines will be used to achieve the desired goal of timely, comprehensive and accurate cancer diagnosis. I urge all stakeholders to support the implementation of these guidelines to enable early diagnosis, improved treatment outcomes and better survival for cancer patients in Kenya.



Sen. Mutahi Kagwe, EGH
Cabinet Secretary
Ministry of Health

Acknowledgements

These guidelines were developed through a multi-stakeholder consultative process involving both the national and county governments' experts within public and private sector institutions. The Ministry of Health wishes to thank all those who participated in the successful development of these guidelines.

We particularly appreciate the support from the offices of the Cabinet Secretary, Principal Secretary, Director General, Director, Directorate of Medical Services, Preventive and Promotive Health, Head, Department of Non-Communicable Diseases for the strategic guidance and support for the development of this document.

We wish to recognize members of the Pillar 2 Technical Working Group of the National Cancer Control Program who worked tirelessly in development of this document. A special thanks to Dr. Shahin Sayed and Dr. Richard Njoroge, the Pathologist supporting the National Cancer Control Program, who put together the technical team that contributed to the development of this document and Dr. Mary Nyangasi, the Head of the National Cancer Control Program for her coordination and guidance role. The contribution of the following individuals is also much appreciated: Dr. Waqo Ejersa, Dr. Njau Mungai, Dr. Catherine Muriithi, Hannah Gitungo, Lydia Kirika, Dr. Eunice Gathitu, Martin Mbaya and Lydia Kirika.

A special appreciation to the Kenyatta National Hospital, Moi Teaching and Referral Hospital, Kijabe Hospital, University of Nairobi, Maseno University, The Aga Khan University Hospital and the reviewers led by Dr. Zahir Moloo from the Aga Khan University Hospital, Nairobi for their professionalism, dedication and commitment in putting this technical document together. We are grateful to Roche and the Clinton Health Access Initiative (CHAI) for their financial support and the Bioventures for Global Health (BVGH) under the African Access Initiative who reviewed the initial draft and provided technical input.

The launch of these guidelines is timely with the implementation of Universal Health Coverage agenda and marks the beginning of a deliberate process to ensure that cancer diagnostics is prioritized in cancer control. I encourage all stakeholders to make use of these guidelines.



Susan N. Mochache, CBS
Principal Secretary
Ministry of Health



Executive Summary

The cancer burden is rising globally, exerting significant strain on populations and health systems at all income levels. In Kenya, cancer is the third leading cause of death after infectious and cardiovascular diseases. The International Agency for Research on Cancer (IARC) as per the GLOBOCAN report of 2018, estimated 47,887 new cases and 32,987 deaths annually. This represents close to 45% increase in incidence compared to the previous report that annual estimated 37,000 new cases with 28,500 deaths in 2012.

The following are the key recommendations of these guidelines.

1. Standardization in the handling of cancer specimens will improve cancer diagnosis, improve accuracy and reduce turnaround time
2. All specimens in suspected cancer cases shall be handled, processed and reported in a standardised manner as provided for in these guidelines
3. Adequate patient consent and institutionalization of specimen referral systems is a prerequisite for all specimen collection described in these guidelines.
4. The fixative 10 % buffered formalin should be made available at all facilities collecting cancer specimens. For standardization, it is recommended that this fixative be processed centrally and be distributed to the peripheral facilities

The goal of these guidelines is to institutionalize a well-coordinated guiding framework for handling cancer specimens for priority cancers to ensure timely diagnosis and linkage to care within the health sector in Kenya.



Dr. Patrick Amoth
Ag. Director General
Ministry of Health





Background

Global Cancer Burden

Cancer incidence and mortality rates continue to rise globally, with an estimated 18.1 million new cases and 9.6 million deaths in 2018. The number of new cases is expected to rise by about 70% over the next two decades, with significant and rising economic effects. The direct and indirect economic costs related to the prevention and treatment of cancer globally were approximately \$1.16 trillion in 2010 (WHO, 2017).

Lung cancer is the most commonly diagnosed cancer (11.6% of the total cases) and the leading cause of cancer death (18.4% of the total cancer deaths) among both sexes combined. This is closely followed by female breast cancer (11.6%), prostate cancer (7.1%), and colorectal cancer (6.1%) for incidence and colorectal cancer (9.2%), stomach cancer (8.2%), and liver cancer (8.2%) for mortality. Globally, among males, lung cancer is leading in incidence and mortality, followed by prostate and colorectal cancer (for incidence) and liver and stomach cancer (for mortality). Among females, breast cancer is the leading type of cancer in incidence and mortality, followed by colorectal and lung cancer (for incidence), and vice versa (for mortality); cervical cancer ranks fourth for both incidence and mortality (GLOBOCAN 2018).

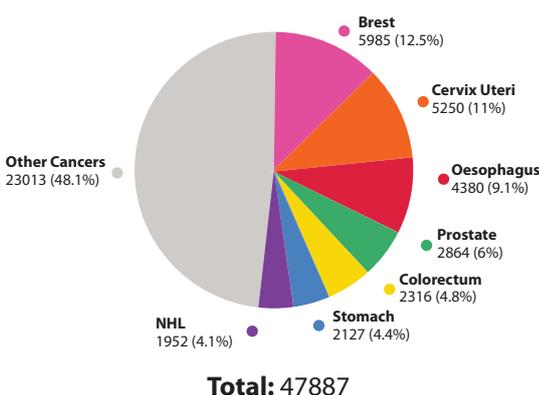
Cancer patterns in different world regions are complex, with the majority of cancers occurring in low- and middle-income countries (LMICs; GLOBOCAN 2018; WHO, 2017). The incidence and mortality for various types of cancer substantially vary across countries and within each country. This depends on the degree of economic development, advancement of healthcare, and associated environmental, sociocultural and lifestyle factors, among others.

Global Incidence & Mortality rates (Age-standardized) for top 10

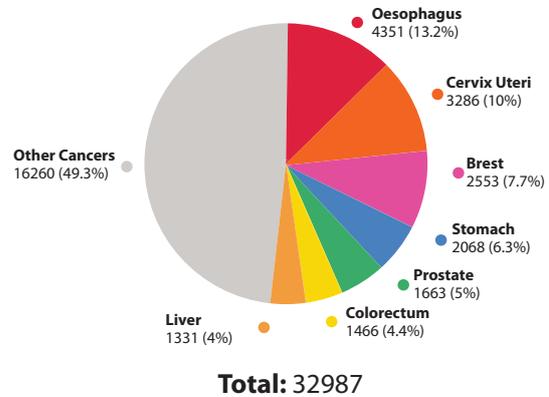
Kenyan Situation

In Kenya, cancer is the 3rd leading cause of death after infectious and cardiovascular diseases. The annual incidence of cancer was estimated at 47,887 new cancer cases, with an annual mortality 32,987 in 2018. Among men, prostate, oesophageal and colorectal are the leading cancers, while among women, breast, cervical and oesophageal cancers are most common. The leading cause of cancer death in Kenya is oesophageal cancer, causing 13.2 % (4,351 deaths) of cancer mortality. Cervical cancer is the second leading cause of cancer death contributing 10% (3,266 deaths), while breast cancer comes in third at 7.7% (2,553 deaths) (GLOBOCAN, 2018).

Estimated number of new cancers in Kenya among all ages, both males & females, GLOBOCAN 2018



Estimated number of cancer deaths in Kenya among all ages, both males & females, GLOBOCAN 2018



One characteristic associated with increased morbidity and mortality related to cancer is late-stage presentation, when cure is difficult to achieve. This is a common problem in Kenya, as is the case in many LMICs (WHO, 2018b), where diagnostic and treatment services are inadequate or non-existent (WHO, 2017). Data from Kenyatta National Hospital show that between 2014 and 2016, approximately 64% of cancer patients were diagnosed at stage III or IV. Many factors contribute to late diagnosis. For childhood cancers, low awareness and stigma amongst parents/guardians and caregivers lead to late presentation of patients to cancer treatment centres (Njuguna, 2016). Additionally, limited diagnostic facilities with insufficient equipment, laboratory consumables and personnel are a challenge.

In an effort to remedy the above-mentioned challenges with cancer diagnosis in Kenya, Pillar 2 of the Kenya National Cancer Control Strategy (NCCS) 2017-2022 focuses on Diagnosis, Registration and Surveillance. Cancer registries are important tools for establishing and maintaining a cancer incidence reporting system, providing information for the investigation of cancer and its causes, and assisting in the planning and evaluation of cancer prevention and control programs. Strategic Objective 2.2 indicates that the Ministry improves and strengthens cancer pathology diagnostic services by developing guidelines for pathology diagnostic workup of priority cancers in both children and adults, among other activities.

Diagnosis of Cancer

There are many techniques and modalities employed in cancer diagnosis, including various imaging modalities. However, tissue diagnosis remains the definitive diagnostic modality, and ordinarily, treatment will not be commenced without a confirmed tissue diagnosis. Tissue diagnosis is a specialist diagnostic service that requires highly trained specialists in pathology, biochemistry, molecular genetics, immunohistochemistry and other fields, as well as skilled laboratory personnel.

Tissue diagnosis requires advanced equipment and laboratory supplies. The specimen is usually tissue, blood or aspiration material. The initial handling for these specimens, irrespective of the tests required, is usually the same. Therefore, standardization of specimen handling is possible.

Specimen handling procedures are straightforward, but because of lack of guidelines and standardization, errors of procedure

occur, resulting in either unsuitability for one or more subsequent tests or inaccurate results. Even though the diagnostic procedure itself may be sophisticated, specimen handling is often simple and inexpensive, and with standardization errors can be minimized or even be eliminated.

Standardization in handling cancer specimens for diagnosis should begin from the time the specimen is obtained and extend to the time the final pathology report is issued. Specimen handling involves a multidisciplinary team of health care workers.

Diagnostic capacity for cancer in the Kenyan Health System

Several reports and surveys have shown the current status of diagnostic capacity in the Kenyan health sector, both public and private. These reports describe the current situation pertaining to medical laboratory diagnosis, in general, and cancer, in particular. With regard to cancer, the reports highlight the current challenges facing the country in actualizing timely and accurate diagnosis. The challenges, among others, revolve around lack of appropriately trained human resources, such as pathologists and technologists, lack of equipment, equipment downtime, lack of standardization, failure to use approved laboratory procedures, unreliable supplies, suboptimal pathology referral and consultation system, and a disconnect in coordinating and running diagnostic services. This has led to a situation where a majority of definitive cancer diagnoses are dispensed from private facilities, and the two national referral facilities (KNH and MTRH) are overwhelmed due to the above-highlighted constraints facing lower-level facilities.

The end result is a haphazard, uncoordinated, inadequately standardized, inaccessible, and expensive cancer diagnostic service that contributes to delayed diagnosis and access to care.

Why are these guidelines needed?

Early diagnosis is associated with better clinical outcomes and prognosis. Accessible, affordable, and effective laboratory services are crucial for early cancer diagnosis. However, guidelines for cancer pathology diagnostic tests are generally unavailable and quality control measures are lacking.

The National Specimen Handling Guidelines will serve as a guiding document for all stakeholders to ensure standardization of specimen handling, processing and reporting using, and evidence-based pathology diagnostic services in Kenya. The guidelines will also enhance coordination of pathology diagnostic activities across the country and allow for more efficient resource allocation.

Who should use the guidelines?

All stakeholders at all levels of care who see patients at risk for cancer should be aware of the National Specimen Handling Guidelines in Cancer Management. Those specifically involved in the pathology diagnostic workup of cancer specimens, including referral of specimens to county or national laboratories, should have particular familiarity with the guidelines. Through an integrated approach, the guidelines facilitate collaboration amongst stakeholder and a common understanding of where they fit in the overall spectrum of cancer pathology diagnosis.





General considerations for cancer specimens

Patient preparation, informed consent and investigation Requisitions

The patient or guardian shall be informed regarding the test indication, specimen collection procedure and process toward laboratory results or report. This discussion shall include costs, expected time lines, and supplementary tests and procedures, when relevant. The patient or guardian shall sign consent upon this discussion. The clinician requesting the test shall liaise with the referral system and laboratory till conclusion of report, including supplementary reports. The primary facility collecting the specimen shall take charge of the initial specimen handling and commitment into the referral system at initial (primary laboratory); it shall receive all reports (first and supplementary) to guide patient management and treatment.

Standard Operating Procedures (SOPs), Manuals, and Forms

Every laboratory must adopt and adhere to national SOPs, manuals, and forms. These shall include the following:

A. Specimen Handling SOP

1. Identification
2. Preparation/consent
3. Requisition
4. Sampling
5. Labelling
6. Laboratory reception
7. Processing
8. Packaging
9. Specimen/Sample referral
10. Transportation
11. Storage
12. Archiving
13. Disposal/ Museum display

B. Reporting and releasing of results SOP

1. Result format
2. Critical values
3. Results communication
4. Confidentiality
5. Storage, archiving and disposal

C. Equipment Management SOP

1. Selection
2. Procurement
3. Installation and commissioning
4. Training
5. Verification and validation
6. Maintenance
7. Retirement and disposal

D. Non-conformance, Corrective and Preventative Action

1. Identification of Non-Conformances
2. Root cause analysis
3. Corrective actions
4. Preventive actions
5. Measurement of effectiveness of CAPA

E. Personnel management SOP

1. Recruitment/ selection
2. Deployment and staff orientation
3. Training and records
4. Competency assessment

F. Ethical conduct SOP

1. Professionalism
2. Conflict of interest
3. Enforcement

G. Commodity and supplies management

1. Selection
2. Procurement/ordering and reception
3. Inventory management
4. Storage and disposal

H. Quality assurance SOP

1. Internal Quality Control
2. External Quality Assurance
3. Interlab Variation
4. Accreditation
5. Customer satisfaction survey

I. Environmental conditions Monitoring SOP

1. Temperatures
2. Humidity

J. Safety SOP

A. Specimen collection and handling at collection site

At the point of collection, the required commodities such as wide-mouthed container, 10% neutral buffered formalin, labelling material, appropriate sutures or dyes for identification purposes, glass slides as appropriate, must be available. The specimen should be fixed immediately (cold ischaemic time) after removal to prevent autolysis and putrefaction and taken to the laboratory immediately. At every specimen sampling point, e.g. theatre, there shall be a standard to guide specimen handling and delivery to the laboratory. This shall include placing orientation features, use of specified containers, fixatives and primary dissection if required, and labelling. Avoidance of crush artifacts shall be observed by gentle handling and use of wide mouth containers.

Tissue shall be placed in specified preservative at earliest encounter to avoid ischemic damage, routinely 10% neutral buffered formalin in a ratio of 1:10 volume (specimen: preservative)



Information on the specimen label must match that on the requisition form. Standardized labels should be used. Minimum data required on the specimen label include the following:

- Last name, First name
- Date of Birth – DD-MM-YYYY
- Outpatient/ Inpatient number
- Ordering physician
- Site of specimen
- Time of fixation

Minimum data required on request form:

- Bio data - patient three names, national identification number, inpatient or outpatient no., date of birth, sex, marital status, patient telephone number and next of kin name and phone number, county of residence, occupation, education level, smoking status, drinking status
- Clinical information – presenting complaints, duration, clinical findings and diagnosis, anatomic site sampled, nature/type of specimen, date and time of sample collection, name and institution of clinician.

Specimen type

This shall depend on the level of care as per the Kenya Essential Package for Health, equipment, personnel and training available to provide the services. At introduction, the referral system shall have a monitoring supervisory and mentoring system. Specimens shall include Exfoliated cell cytology samples such as urine, peritoneal and pleural space aspirates, sputum and bronchial washes, etc. as necessary for body region or system

cancer diagnosis, staging and management. These shall be collected in specified containers and /or smear slides

Other specimens shall depend on organ, system and suspected pathology as specified in relevant sections of guideline; examples fine needle aspirates (FNA), cervical smears and wound impression smears, cavity and cyst curetting’s, endometrial curetting’s and biopsy, wound edge biopsy, lumps and small masses excisions, incision biopsies, bone marrow aspirates and biopsy, other organ and system biopsy types per surgical procedure.

All tissue material removed from body should be subjected to histology evaluation. These include tubal and bowel resections, abscess curetting, appendectomies, bone resection and fragments, etc. Exception of the tissues that are not sent to the laboratory, e.g teeth, lens removed for cataracts, etc., must be authorized by the respective hospital medical advisory committee or equivalent authority.

Where partial specimen processing is possible, activities to be performed shall be pre-determined such that consultation structure are tailored to maximize local capacity referring only what is necessary. An example is when there is capacity for sample collection (biopsy), tissue processing and slides preparation and staining, but no microscopy reporting, only stained slides for reading/reporting is be outsourced or referred into the referral system.

Level of Health Care	Suspected Cancer detection Specimen
Community Health Care Level – previously level 1	-
Primary Health Care Level (Dispensary and Health centres) – previously levels 2 and 3	-
Secondary Health Care Level (County Referral Hospitals) – previously levels 4 and 5	FNA/ Exfoliative Cytology, Biopsies, Resection specimens, Bone Marrow Aspirates
Tertiary Health Care Level (National Referral Hospitals) – previously level 6	All the above plus Molecular tests, Immunohistochemistry, Genetics, Liquid Biopsies

Frozen sections

Should be done only at specialized centres and cross consultation required in its total planning and implementation.

Specimen receiving

Specimen received into laboratory system shall have a minimum of two unique identifiers and label to be used throughout processing and reporting and committed to a tracking system. The hospital bears the responsibility of the specimen handling and NOT the patient. All the personnel handling the specimen at all levels including transportation shall be documented and movement logs provided. Transport of specimens to the laboratory needs to occur as soon as possible and in cognizance of initial handling and referral system logistics to prevent delays in specimen processing. At reception, the specimen shall be evaluated against acceptance rejection criteria and preserved with appropriate fixative unless its prior done.



Specimen rejection

It is important to establish criteria for rejection and equally important to define what happens if those criteria are met. In other words, laboratories must uphold strict standards for the conditions under which specimens will be accepted, but there must also be a mechanism in place to allow any deficiencies to be corrected before a specimen would potentially be discarded. Essentially, all efforts should be made to analyze all specimens obtained from suspected cancer patients and limitations addressed. The requesting clinician/institution shall be contacted immediately regarding possible rejections.

Specimen grossing

Every laboratory conducting grossing must have an appropriately-sized grossing station, including a sink and a biosafety hood with adequate ventilation. Specific recommendations for grossing techniques are provided in the various cancer type sections in this guideline and SOPs. Laboratories should create a grossing job aids that are easily accessible at the grossing station.

Specimen reporting/Communication of final report

Synoptic reporting should be used, especially for ALL cancer resection specimens. This includes presence of cancer, histology type and grade, completeness of excision, involvement of margins, nerves, vessels, and lymph-nodes. These synoptic reports can be downloaded for free from the College of American Pathologists website (www.cap.org).

Turnaround time for cytology, bone marrow aspirates and histology shall be within 7 days and 14 days respectively. For ancillary tests that might be required, a preliminary histology report can be issued in the meantime.

When results are ready, they should be promptly dispatched to the requesting clinician by designated appropriately-qualified professionals. Professionalism should be upheld by clinicians communicating between themselves. Results should preferably be reported online for ease of accessibility by the requesting clinician. A hard-copy should follow and a scan or photograph of the same may be electronically transmitted. Hard copy of the results should be archived in the laboratory. A standardized final report form template is provided in Appendix.

The requesting clinician is responsible for communicating the results to the patient. This should ideally be done in person with appropriate counselling services provided, along with recommendations for treatment and follow-up.

Ancillary testing should be encouraged where resources permit, so as to generate as much possible diagnostic information for optimal and individualized treatment. An integrated specimen referral system for specimens requiring ancillary testing is recommended.

Specimen archiving

The processed sample should be appropriately archived to allow easy retrieval if a second opinion or further tests are required. Each of the histology laboratories should have SOPs for storage of specimens. Gross specimens, 3 months after final report is issued, paraffin tissue blocks 10 years indefinitely, stained slides 20 years, and final reports indefinitely. The SOP should also include information regarding disposal of the specimens and slides when required retention period is expired including release for research and museums. Any archived specimen belongs to the patient and should be made available on request. Any sample issued to the patient should be documented for accountability and medico-legal purposes.

Specimen referral

Effective communication is needed in referral networks to ensure efficient service provision. Documentation requirements should be defined and applied, including the satellite laboratory, collection points, the courier identity, and the referring laboratory. Standardized requisition forms should be used and must be completed accurately. Contracts/agreements should be in place for incoming referrals, outgoing referrals, and courier services. Specimens should only be transported by an approved and recognized courier service.

Specimen packaging

Often ground overnight shall be anticipated for FFPE samples, and packaging shall conform to IATA guidelines even if transported via ground courier. A completed sample requisition form (Appendix 1) and a material transit instruction form (Appendix 2) sample requisition shall accompany the specimen during transport. The material transit instruction form shall detail the expected transit conditions such as avoidance of breakages, spillage, spoilage (fragility, breakable, what side up, containment temperatures, etc.) by practice and use of labels.

The standard protocol for packaging should be used that includes triple packaging and sturdy containers, transparent glass and plastic preferred. The lab should stock different sizes of containers and liaise with the operating theatres for sample packaging containers procurement, distribution and user training.

Provision and standards shall be made regarding handling instructions for specimens in transits. These concern biohazard warning, fragility, transits temperatures, liquids contents (which side up) These shall be attached to packages and training done for all handlers.

Breast Biopsy Container Sizes



Referral Sustainability

Sustainability shall be entrenched in contractual agreements apportioning distribution of resource and liabilities, considering fairness in remuneration of personnel and institutions.

An inventory of all laboratories, their capacities, and investigation types menu shall be maintained and reviewed annually. Referral networks shall be determined by these capacities and procurement contractual agreements.

Contributions of institutions of higher learning (University Teaching Hospitals, Research institutes as KEMRI, and tertiary Hospitals, independent and private specialized laboratories, etc.) as terminal professional consultative forums shall be factored in recognition of their position as service providers, local and regional experts in clinical -research implementation. Their position shall be factored in referral strategy planning and public external (international) outsourcing.

Logistics needed to manage specimen movement

These shall ensure SOPs on sample handling are adhered to as appropriate for site, and documented as necessary.

Service Unit	Basic Logistics Needed for Specimen Movement		
	Human Resources	Commodities, Supplies, Equipment	Means of Communication
Community Units	Community Health Extension Workers	<ul style="list-style-type: none"> Standard operating procedures for specimen collection, package, and movement Personal protective clothing Appropriate specimen containers and transport media 	Motorised bicycle and motorbike, telephone
Primary Care	Nursing officers, Medical laboratory technologist and technician	<ul style="list-style-type: none"> Standard operating procedures for specimen collection, package, and movement Personal protective clothing Basic laboratory supplies Appropriate specimen containers and transport media 	Motorbike and bicycle, prepaid and contractual courier services, telephone
County Referrals	Nursing officers, Clinical and Medical officers, Medical laboratory technologist, health records, and information officers	<ul style="list-style-type: none"> Standard operating procedures for specimen collection, package, and movement Personal protective equipment Comprehensive laboratory supplies Appropriate specimen containers and transport media IT infrastructure and capability 	Motorbike and utility vehicle, pre-paid and contractual courier services, telephone
National Referrals	Laboratory technologist, health records, and information officers	<ul style="list-style-type: none"> Personal protective equipment Comprehensive laboratory supplies Appropriate specimen containers and transport media IT services (movement of results and reports) 	Motorbike and utility vehicle, international courier, telephone

Laboratory specimen referral, as an integral part of the health care system, requires monitoring and evaluation. It incorporates routine collection and tracking of key data on the performance of a system to help identify problems in time for prompt correction. The identification of key network performance indicators and maintenance of records and information at all levels in the referral system is mandatory to ensure effective implementation of planned activities. Administrator or appointee shall identify Performance indicators of the referral network to be routinely be monitored to establish its efficiency and effectiveness. Evaluation of data is useful in decision making and quality improvements.

Indicators for the laboratory referral networks to include:

1. Network effectiveness
 - Number of samples sent from satellite sites
 - Number of samples sent to other facilities
 - Number of samples processed completely at site
 - The specimen rejection rate
2. Turn indicators
3. Quality assurance - Internal Quality Control (IQC) and External quality assurance (EQA) performance
4. Proportion of counties with enabling information Technology infrastructure to support referrals
5. Number of Personnel and cadres oriented and trained in specimen referral guidelines

The specimen management SOP shall be adhered to at all points.

Equipment Management

Proper laboratory equipment management ensures that appropriate equipment is procured, used, maintained and serviced following recommendations of quality policy manual for medical laboratory services in Kenya. These include reference materials, reagents, consumables and requisite computer programs/packages.

Basic consideration for equipment should be continuous service availability (zero-downtime), efficiency in resources utilization, sustainability and customer satisfaction.

The laboratory management shall manage equipment inventory and ensure all equipment have a management scheme from initial procurement, commissioning, training, maintenance and repair (a M&R logo shall be kept), materials and reagents supplies, and a retirement/ replacement plan at end of its economic life.

Anticipated catchment workload determines initial equipment procurement with expansion and additions coming with experience and technologic advancements. Automation is necessitated by need to improve turnaround time, maintain customer satisfaction, safety and accessibility to the service.

Laboratory equipment need is dependent on Service delivery level, work load, personnel training and availability of materials and supplies; it's all directed to efficient utilization of resources to provide quality services that meet client satisfaction. For example, if quality and reliable ready to use distilled water, stains and reagent can be economically outsourced, corresponding basic equipment such as water distillers, stains and reagent preparation platforms, etc. can be omitted.

Some others as centrifuges, safety (hoods) chambers, tissue processors, microtomes and slide strainers are of variable manner and capacities, their procurement therefore highly individualized. Examples are that aspirate fluids from pleural and peritoneal cavities, bronchial-alveolar lavage and other cytology material when cancer is suspect. Their potential differentials diagnoses are communicable infective diseases as fungi and mycobacterial thus requiring class 1 safety cabinets for processing. Similarly, many cell suspensions, watery lavages and fluids require concentration before transfer to slides while cyto-centrifugation may be used for low cellularity fluids as urine and CSF. Effusion and curettage material can be used to make cell blocks for histology. All these activities require specialized equipment whose capacity depend on catchment area and workloads.

All procured critical equipment shall be validated and commissioned on site and necessary training /induction of staff done simultaneously.



Human Resource



Human resource management policy guiding implementation standard operating procedure shall be employed at all levels

Skills and Cadres

Appropriately trained personnel, registered and licensed by their certified regulatory boards, and deployed in licensed participating Institutions shall be expected to work, adhering to national and international guidelines on skills, qualifications, numbers required and licensing requirements for each level of care. Deployment, orientation, capacity building, continuous improvement/competency testing shall be employed as appropriate for all staff cadre; surgeons and other clinicians, pathologists, histo-technologists, cytotechnologists, hematopathology technologists, Laboratory scientist, transporter and courier system and logistics personnel.

Laboratory safety

Laboratory procedures involve specimen collection, transportation and processing which pose a risk to the specimen itself, the handlers and environment. Good biosafety and biosecurity practices ensure that the laboratory worker, safety of the specimen and the environment are protected. Biosafety measures in referral networks shall comply with the universal safety precautions, waste segregation, and disposal protocols. Laboratories should carry out bio-risk assessments to identify risk factors associated with the integrated specimen referral networks. Each laboratory in the network shall have a biosafety officer who will coordinate all matters pertaining to biosafety and biosecurity practices including safety audits using standard checklists.

Quality assurance (QA)

Laboratories in the referral network should adhere to good laboratory practices. Laboratories should have a Quality Manager/Officer who is responsible for developing and executing a Total Quality Management (TQM) system consisting of internal quality control (IQC), external quality assurance (EQA), and continuous quality improvement (CQI). An SOP for non-conformance, corrective, & preventative action and root cause analysis (RCA) should be included as part of the TQM system. Establishing a TQM system reduces the chances of variability in the laboratory processes, testing and reporting.

Accreditation

Accreditation should follow ISO Standards and any other internationally or nationally recognized standards.

Audits

Internal and external audits

Multidisciplinary Tumour Boards (MDT) approach/tele-tumour boards Multidisciplinary tumour approach should be active in patient management and should include different specialties, including pathologists.

Ethical Practice

Appropriate technical practice and integrity in attitudes and behaviour in reference to moral values, is an integral part of quality laboratory practice. In suspected cancer cases and post diagnosis follow up management of cancer patients, an invalid result can be misleading and a liability to the entire patient management system, even occasioning direct harm. Dangers include loss of life, delayed treatment, litigation and financial implications. Invalid results statistics are misleading in improvement projection, jeopardizing current and projected planning process.

Pathologists, laboratory scientists, clinicians and participants in the specimen referral process are duty bound by values, ethical codes and regulations of their registering bodies. Concerns of

ethical practice in cancer patient management include illegalities and actions contrary to conscience. The range is wide including personnel deployment, training, quality equipment, reagents and supplies, confidentiality and release of reports, information management, sub-optimal standards in health delivery, service fees and costs, etc.

The health system to which a patient prescribes needs to be a protector as asymmetry exists regarding knowledge of disease in patient-doctor relationship from inception of service planning guiding informed consent(s), range and choice of investigations/tests and their anticipated benefits, alternatives in disease management, costs and expectations in direct and third party payers, including whether and where to refer for other management.

The sample referral system has ethical obligation at many levels in addition to patient and guardian as it relates to clinicians and professional colleagues, institutions, and society. In all respect the autonomy of the patient/guardian, duty to act in patient's best interests, to do no harm and remain in fairness, equity and justice to society at large.

All aspects of laboratory practice in diagnosis and later management of cancer patient shall have ethics embedded in quality service delivery.

A monitoring and corrective system shall be maintained with deliberate interaction with all professional bodies of involved participant

A deterrence method provided for unethical behaviour shall:

- 1 Develop an ethics policy and add it to the laboratory's quality assurance manual.
- 2 Develop and implement an ethics training program for laboratory analysts.
- 3 Develop a fraud detection and deterrence program
- 4 Incorporate individual analyst log-in for instrument operation and data entry available at all computer and software audit trails
- 5 Have known penalties for non-compliance
- 6 Introduce and maintain training and adherence to the laboratory standard operating procedures and the promulgated method
- 7 Have a strong TQM program with complete data review, and QC summary sheet review with transcriptions review
- 8 Introduce and maintain Periodic data package review including electronic file reprocessing.
- 9 Review of all audit trails and manual integrations

References

- Role of the National Oncology Reference Lab
- Licensing and regulation – Reference Health Act 2017
- Regulatory bodies – roles of KMPDB & KMLTTB
- Listing of accredited and recognized labs
- Research – access to samples, ethics
- Roles and responsibilities of various stakeholders from NCCS 2017-2022
- Kenya Health Sector Referral Strategy 2014-2018. Ministry of Health
- National Guidelines for Cancer Management Kenya, 2013.



Breast



Introduction

Sub-optimal fixing, handling and processing of breast specimens has been a chief source of inadequate pathology reports. Tissue handling including that of 10% neutral buffered formalin-fixed, paraffin-embedded (FFPE) tissue has a significant impact on the quality of intercellular and intracellular components, which may affect results of analyses performed on those specimens.

With regard to breast specimens, these guidelines seek to:

1. Promote and ensure proper collection of high-quality tissue specimens such that each patient diagnosed with breast cancer can have a reliable, interpretable routine and molecular diagnosis;

2. Provide a known baseline of standardization of specimen collection and handling procedures, to the extent possible, such that more ancillary testing will be possible; and,
3. Promote specimen collection that would allow for future technologies, particularly in the molecular arena, to be applied to these specimens for future applications.

Fresh/frozen tissue collection is susceptible to limited timelines for acceptable collection. However, as long as the general principles of rapid collection and freezing, as well as seamless integration with standard pathologic assessment are observed, these collection and analysis can be accomplished.

The table below shows specimen types and appropriate fixation

Procedures	Specimen	Personnel Responsible for specimen collection	Diagnostic Utility	Level of facility	Fixative	Specimen Adequacy	Comments
FNA	Aspirate	Cos, MO, surgeons, Pathologists	To assess lymph node involvement prior neo adjuvant chemotherapy For metastatic lesions that are amenable to procedure For multifocal disease For recurrent breast cancer at site of previous scar	Level 4, 5 and 6	95 % ethanol	2-6 slides, each with 3 minimum clusters	Only if Neo adjuvant treatment will be offered
Nipple Discharge smears	Smear imprint/ touch cytology	Cos, MO, surgeons, Pathologists	For assessment of nipple pathology e. g benign papilloma versus malignant lesions	Level 4, 5 and 6	95% ethanol and air dried	Minimum 2 slides	Initial evaluation of nipple lesions
Wound impression Smears	Touch/ imprint smears	Cos, MO, surgeons, Pathologists	A quick guide to diagnosis –	Level 4, 5 and 6	95% ethanol and air dried	Minimum 2 slides	can be as an initial test used to triage breast lesions
Wound excision/ ulcer edge biopsy	Tissue biopsy	MO, surgeons	For definitive diagnosis and ancillary testing	Level 4, 5 and 6	10% NBF	Minimum 0,5 mm	
Core biopsy	Core tissue biopsies	MO, Surgeon Radiologist	Recommended primary diagnostic modality, grading, biomarker analysis	Level 4, 5 and 6	10% NBF	3-5 cores, 10-20 mm each	Fix immediately within one hour for 6-72 hours in 10X volume of specimen. Note: Good cores will sink in the fixative



Procedures	Specimen	Personnel Responsible for specimen collection	Diagnostic Utility	Level of facility	Fixative	Specimen Adequacy	Comments
Lumpectomy	Tissue excision biopsy	Surgeon	Definitive tissue diagnosis and treatment	Level 4, 5, 6	10% NBF	Adequate margin	immediately for 6-72 hours in 10X volume of specimen Primary Excision biopsy of breast masses should only be considered when core biopsies are none revealing or inconclusive
Total Mastectomy +/- Lymph nodes	Whole Breast	General Surgeon or specialist breast surgeon	Definitive treatment for Extensive DCIS	Level 4,5,6	10% NBF	Adequate margins and slicing through tumor form skin surface	Fix immediately within 1 hour for 24-72 hours in 10X volume of specimen
Wide local excision (Excision less than total mastectomy), +/- Lymph nodes	Wide excision	Breast surgeon	Breast conservation	Level 6	10% NBF	Adequate margins	Fix immediately for 6-72 hours in 10X volume of specimen Radiotherapy Services available
Sentinel Lymph node	Either mastectomy or Breast conservation surgery	Breast Surgeon	Staging, determines further treatment	Level 6	10% NBF	Up to 2-3 lymph nodes	Used in clinically none palpable lymph nodes Safety precautions to be enforced
Mastectomy Post neo Adjuvant therapy +lymph nodes	Completion surgery post treatment	Breast surgeon	Response and staging	Level 5 and 6	10% NBF	Breast and adequate axillary lymph nodes	Reported according to post neo-adjuvant protocols (Appendix 3) Fix immediately for 6-72 hours in 10X volume of specimen
Fresh /Frozen Tissue	Margins, sentinel node	Breast surgeon	Margin assessment and sentinel node involvement Tissue banking/ clinical trials	Level 6	Liquid Nitrogen/ or store at -80 Degrees	Margins appropriately labeled Dependent on Study protocol	Safety precautions to be enforced

Further Considerations

1. FNAB/C specimens can also be used for cell block preparations for ancillary testing
2. Image-guided core biopsies should be done for all breast lesions.
3. Cytology of nipple discharges, wound impression smears and wound edge biopsies may be of value for initial assessment
4. In cases of Total Mastectomy and excisions less than total mastectomy, the surgeon should indicate the specimen laterality and orient the specimen for gross pathology trimming using long suture for lateral and short suture for superior surfaces. The container used should be wide mouthed and leak proof, where the specimen floats without squeezing to ensure easy retrieval.
5. The pathologist should section the specimen in 5 mm thick sections in the axis perpendicular to the long axis.

NOTE: *If there will be a delay in grossing of the specimen due to transportation to a referral laboratory the surgeon/medical officer shall ensure that the specimen is properly sliced before immersion into 10% neutral buffered formalin.*

Pathology Grossing of the breast

The general guidelines in grossing breast samples are applicable to all histology and are below expounded for specific breast handling procedure.

1. Use the axillary tail and skin to orient the specimen
2. Ink the deep margin
3. "Bread-loaf" at 5mm intervals
4. Submerge in the 10% neutral buffered formalin(NBF) for a minimum of 8 to 12 hours
5. The recommended maximum fixation time is 72 hours

Examination of the Specimen

The following should be recorded and described:

1. Dimension of specimen and skin ellipse
2. Localization, dimension of tumor
3. Margins of tumor
4. Distance from overlying skin deep and closest margin
5. Surrounding breast, Nipple areola and overlying skin
6. If previous biopsy site/cavity present, describe, appearance and location. Also note the presence of any residual tumor

The diagram below shows a breast specimen before and after sectioning as recommended





Handling of Axillary lymph node dissection

A minimum of 10 axillary lymph nodes are recommended for adequate axillary dissection specimen. Each node should be submitted in a separate tissue cassette. For grossing purposes, an abnormal node should be bisected and one half submitted. Nodes equal to or smaller than 5 mm should be submitted in whole.

http://webapps.cap.org/apps/docs/committees/cancer/cancer_protocols/2012/BreastInvasive_12protocol_3100.pdf

Handling of Sentinel lymph node

In the event that sentinel node examination infrastructure is in place, specimen nodes brought to the laboratory must be sliced at 2 mm interval and touch imprints and scrape cytology can be performed as well as frozen sections for pathologist review. Each 2 mm permanent section of the node/s should be examined.

<https://www.archivesofpathology.org/doi/pdf/10.5858/arpa.2015-0140-RA>

Minimum data set for breast (Appendix 1)

Lab SOPs (Link to practical handling of surgical specimens by CAP))

Pathology report synoptic format Appendix 2 ([Link to http://webapps.cap.org/apps/docs/committees/cancer/cancer_protocols/2012/BreastInvasive_12protocol_3100.pdf](http://webapps.cap.org/apps/docs/committees/cancer/cancer_protocols/2012/BreastInvasive_12protocol_3100.pdf), RCPATH,)

Tumour type
 Presence/absence of DCIS.Extent
 Skin/Skeletal muscle status
 Pathological stage (TNM)

Ancillary Testing

It is now recognized that breast cancer is a heterogeneous disease genetically despite similarity in clinical presentation. These cancers have different treatment modalities and outcomes. Ancillary testing assists the pathologist and clinician in arriving at the exact phenotype, hence individualizing treatment modalities.

The table below shows the main biomarkers performed on breast specimens in ancillary testing:

Biomarker	Method	Indication	Preferred Specimen	Utility
ER	IHC	Routine	Core biopsy	Predictive and prognostic
PR	IHC	Routine	Core biopsy	Predictive and prognostic
HER 2	IHC/FISH/DISH	Routine	Core biopsy	Predictive and prognostic
Genomic (Recurrence Score)	Oncotype DX, PAM450	Early breast cancer ER/PR positive, HER2 negative,	FFPE specimen	Risk of recurrence and predictive
BRCA 1 and 2, PALB mutations	Molecular	High Risk family history, young patients	Saliva, Blood	Identification of high risk and prophylactic therapy

Breast specimen/BCT margin evaluation

<https://www.archivesofpathology.org/doi/pdf/10.5858/arpa.2016-0626-CP>

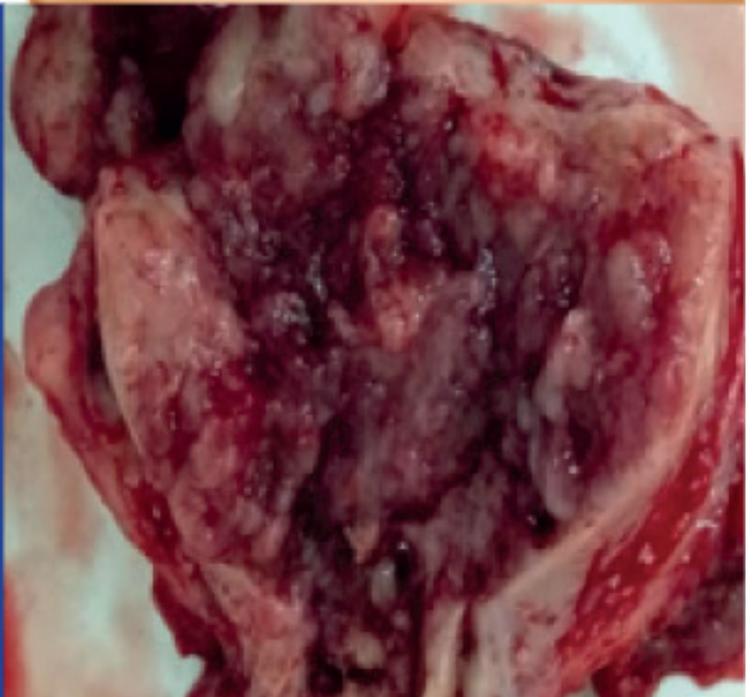
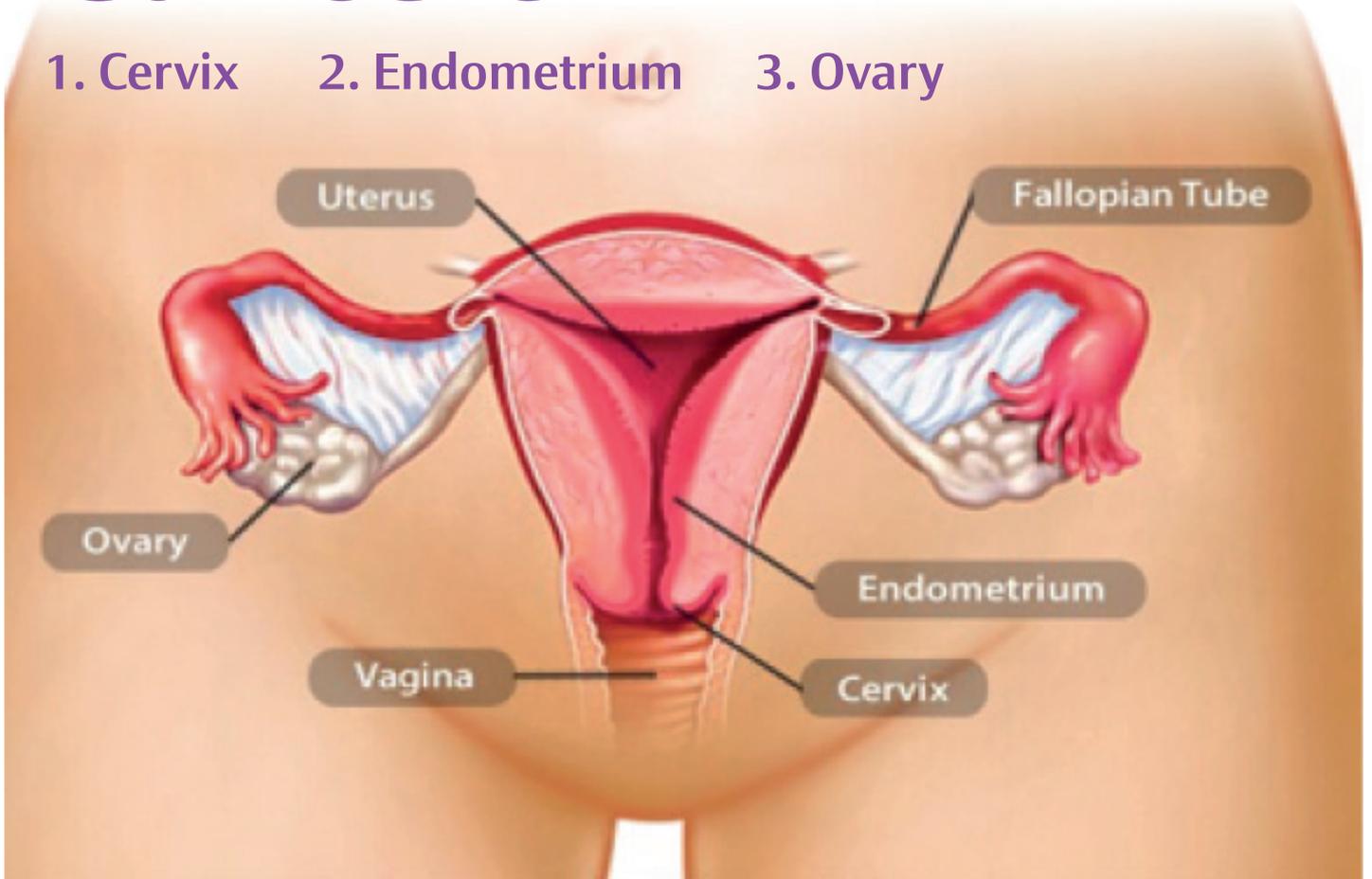
http://webapps.cap.org/apps/docs/committees/cancer/cancer_protocols/2012/BreastInvasive_12protocol_3100.pdf

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1. Recommendations for Collection and Handling of Specimens From Group Breast Cancer Clinical Trials <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2651095/>
2. 2002 Standards, Options and Recommendations: good practice for the management and shipment of histologic and cytopathological cancer specimens.
3. Lester, S. (2010). Manual of Surgical Pathology (3 ed.). Saunders: Elsevier Inc.
4. Westra, W., Hruban, R., Phelps, T., & Isacson, C. (2003). Surgical pathology dissection an illustrated guide. (2 ed.). New York: Springer-Verlag.
5. Tidiane, E. (n.d.). Surgical pathology grossing manual abq health partners pathology. Retrieved from <http://www.pathabqhp.com/files/55810223.pdf>
6. Qu, Z., Anders-DiPonio, M., Ghorbani, R., & Le, M. (2013). E-manual for specimen gross examination in surgical pathology. (3 ed.). NuoNuo Medical Informatics, LLC. Retrieved from <http://www.essentialpathology.info/>
7. Robert Lott, Janet Tunnicliffe, Elizabeth Sheppard, Jerry Santiago, et al Practical Guide to Specimen Handling in Surgical Pathology

Gynaecologic Cancers

1. Cervix
2. Endometrium
3. Ovary





A: CERVIX

In order to accurately diagnose cervical cancer, the following samples are usually collected and submitted to the laboratory for analysis:

- i. Cervical smears (Conventional Pap smears and/or Liquid-based cytology & HR HPV detection)
- ii. Punch biopsy
- iii. Cone biopsy
- iv. LEEP/LLETZ biopsy
- v. Hysterectomy

Table 1. Types of cervical biopsies and respective handling

Specimen type	Nature of sampling	Personnel	Laboratory handling
Cervical Smear Cervical (Pap) smear	1. Conventional alcohol fixed smear on a glass slide 2. Cervical sample in a liquid based medium 3. Self-collected	Trained healthcare worker, Self-collection (HPV)	All processed
Punch biopsies	Few mm, from visible cervical lesions during screening (VIA/VILLI), Colposcopy and EUA	Gynaecologist Trained MOs/Cos	All processed
LEEP/LLETZ biopsies	Electrocautery excisions of the cervical transformation zone Submitted separately as Superficial and Deep	Gynaecologist	Superficial and Deep tissues processed separately
Cone biopsy	Conical excision of the cervical canal (laser or cold knife excision).	Gynaecologist	All processed sequentially (As per protocol below)
Radical Hysterectomy	Removal of uterus, cervix, vaginal cuff, parametria and regional lymph nodes (Left, right pelvic & paraaortic) Nodes submitted separately (in labelled containers- L, R, P)	Gynaecologist	Processed as per protocol below

1. CERVICAL (PAP) SMEARS

i. Conventional smears

Requirements for sample collection: Fixative (Absolute alcohol), Cyto brush, Microscope glass slide, speculum
Fixation in absolute alcohol immediately
Sample and properly filled requisition form are submitted to laboratory for processing.

Papanicolaou staining is done as per SOP (Appendix) Slide is examined and reported (Appendix report format) Report is submitted to requesting clinician

ii. Liquid based preparation

Brush/swab placed immediately in preservative liquid medium
Sample submitted to laboratory for processing
Cytospinning and cells concentrated
Smears are PAP stained or analyzed for HPV

2. PUNCH BIOPSY

Once collected the sample is immediately fixed in 10% NBF
Allow fixation for a minimum of 6 hours
Sample is grossed – Number, size(s), colour and general Appearance
Processing, embedding, sectioning and staining is done as

per SOPs
Examination and Reporting
Dispatch of results to requesting clinician

3. CONE BIOPSY

A cervical cone biopsy is a conical excision of the cervical canal performed with either a laser or a surgical blade (cold knife excision). The wider part of the cone is the outer ectocervix, and the tapered end is the endocervical margin.

- Orientation-By convention, the ectocervix is described as a clock face with the most superior midpoint of the anterior lip designated as 12 o'clock. This point is usually marked with a stitch by the gynaecologist
- Measure
 - i. the length of the cone biopsy corresponding to the endocervical canal,
 - ii. the diameter at the ectocervical margin, iii. the diameter at the endocervical margin
- In the exposed fibrous stroma and the ectocervical mucosal margin. Use a different colour to ink the endocervical mucosal margin.



- Make a longitudinal incision through the outer stroma to the inner canal at the 3-o'clock position, and open the specimen so that the inner mucosal surface is exposed.
- Examine the mucosal surface, and look for any lesions, especially along the squamocolumnar junction.
- Cut serial full-thickness sections perpendicular to the mucosal surface in the plane of the endocervical canal. The sections should be 0.2 to 0.3 cm wide and will end up being slightly wedge-shaped.
- All sections should be submitted sequentially and designated as to their clock-face orientation, i.e. 12-3, 3-6, 6-9 and 9-12 o'clock. Submit a maximum of one to two sections per block.

4. RADICAL HYSTERECTOMY

Sample collected from surgical treatment of early cervical cancer

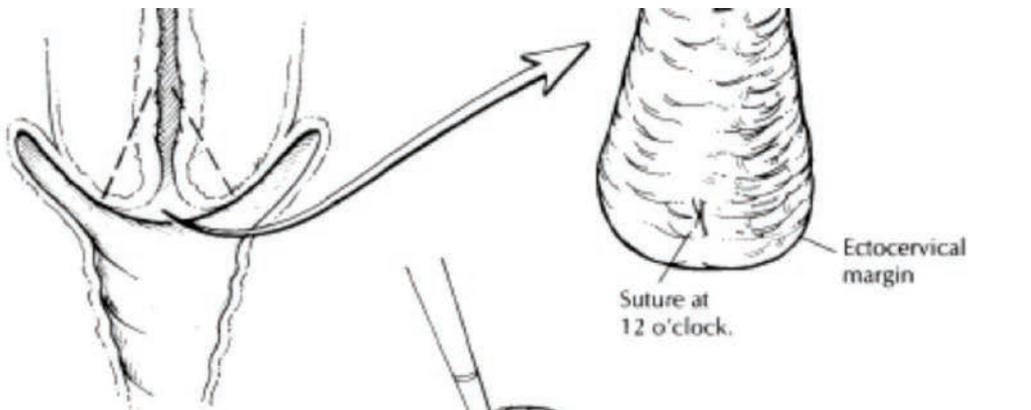
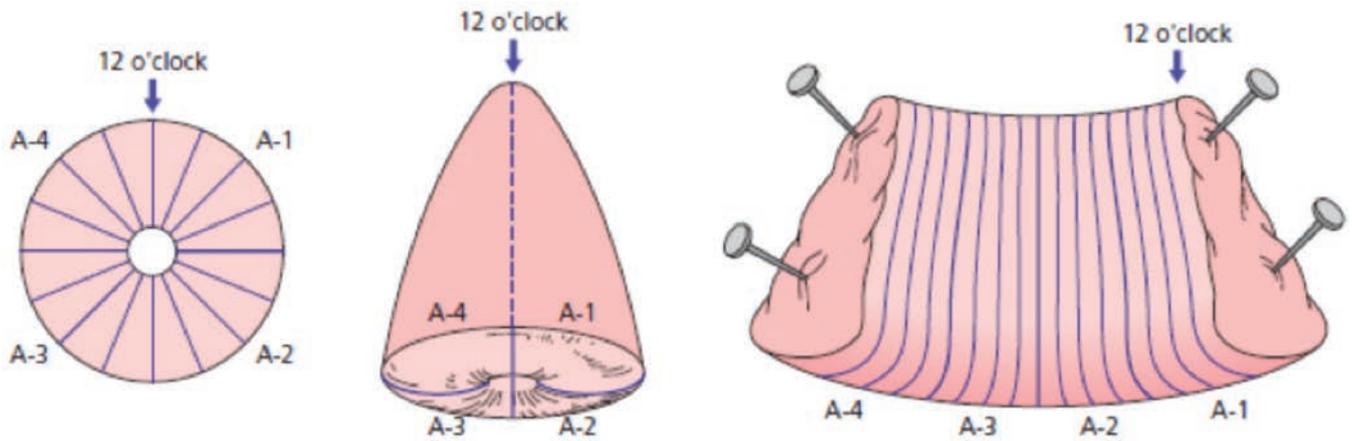
- Begin by orienting, measuring, and weighing the uterus and cervix
- Measure the size of the attached parametrial/paracervical tissue and length of the attached vaginal cuff.
- Ink the right and left parametrial/paracervical tissues, the anterior/posterior soft tissue margins of the cervical canal, and the vaginal cuff margin.
- Remove the parametrial/paracervical tissue by shaving each side close to its lateral attachment on the cervix. Thereafter, section the tissue at 3mm intervals, and submit the entire tissue for histologic examination.
- Any identifiable lymph nodes may be dissected and separately designated.
- Amputate the cervix at the level of the internal os, and open the canal with a longitudinal incision opposite the tumour. (Pin it open, and fix it as you would a cone biopsy.)
- Measure the maximum tumour width and length as well

as the distance to the nearest vaginal margin. Examine the vaginal cuff. Unless the tumour is close to the vaginal margin, the margin may be removed with 3mm parallel shave and submitted as four designated quadrants.

- If the tumour closely approaches the vaginal margin, leave the vaginal cuff intact and take perpendicular margins to demonstrate the relationship of the tumour to the margin.
- Serially section the cervix at 3mm intervals and measure the maximum tumour thickness as well as the thickness of the cervical wall at that site.
- Take a transverse section of the lower uterine segment and bivalve the uterus into anterior and posterior halves. Examine the corpus with serial transverse sections
- Take representative sections from superior extent, inferior extent, and parametrial/paracervical and vaginal margins for microscopic analysis
- The anterior and posterior cervical soft tissue margins should be submitted to delineate the extent of the tumour in relationship to the bladder and rectum.
- Lymph nodes are usually submitted from the right and left pelvic nodes and para-aortic node groups.

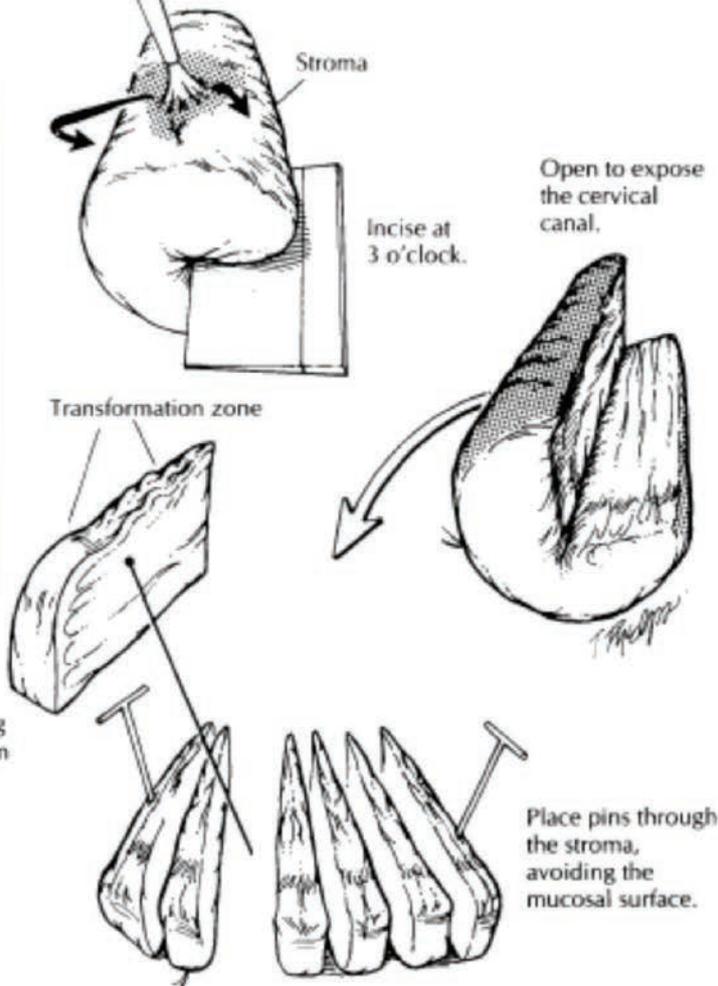
Surgical Pathology report – minimum dataset

Procedure Tumour size Histologic type Histologic grade
Depth of invasion
Paracervical tissue/vaginal cuff/parametrial involvement
Lymphovascular invasion
Pelvic Lymph nodes – Left, Right & para-aortic –
-Number involved, Extranodal extension
Margins status-Parametrial (Left/Right), Vaginal Cuff,
pathological staging



Cone Biopsy

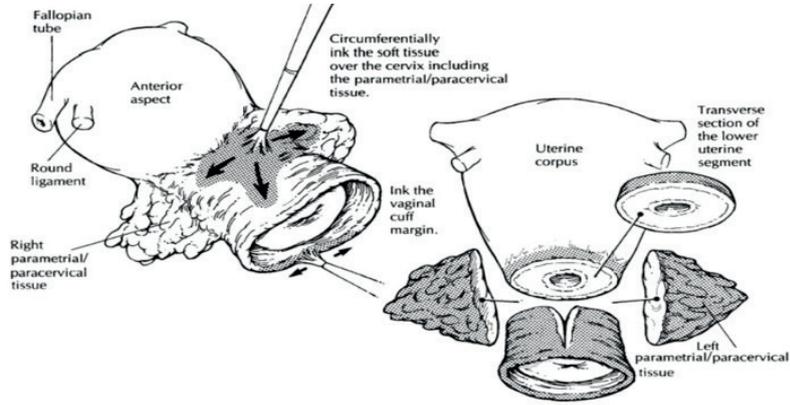
1. Orient the specimen with the stitch at 12 o'clock.
2. Ink the endocervical margin and the stromal/ectocervical margins with separate colors.
3. Open at 3 o'clock, pin on a wax or cork board, and fix.
4. After fixation, take serial, 2- to 3-mm-thick sections as shown.
5. Submit the entire specimen sequentially. For example, block A = two sections from 12 to 3 o'clock; block B = two sections from 3 to 6 o'clock, etc.



Section demonstrating a continuous line from the ectocervix to the endocervix

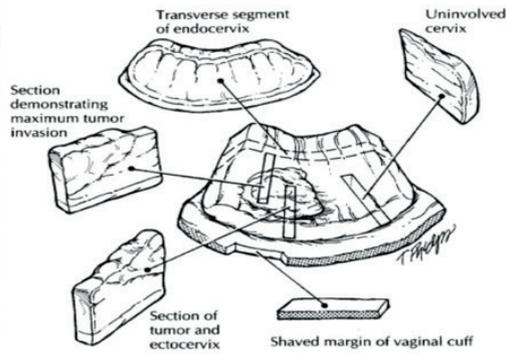
Place pins through the stroma, avoiding the mucosal surface.

Maintain the clock-face orientation.



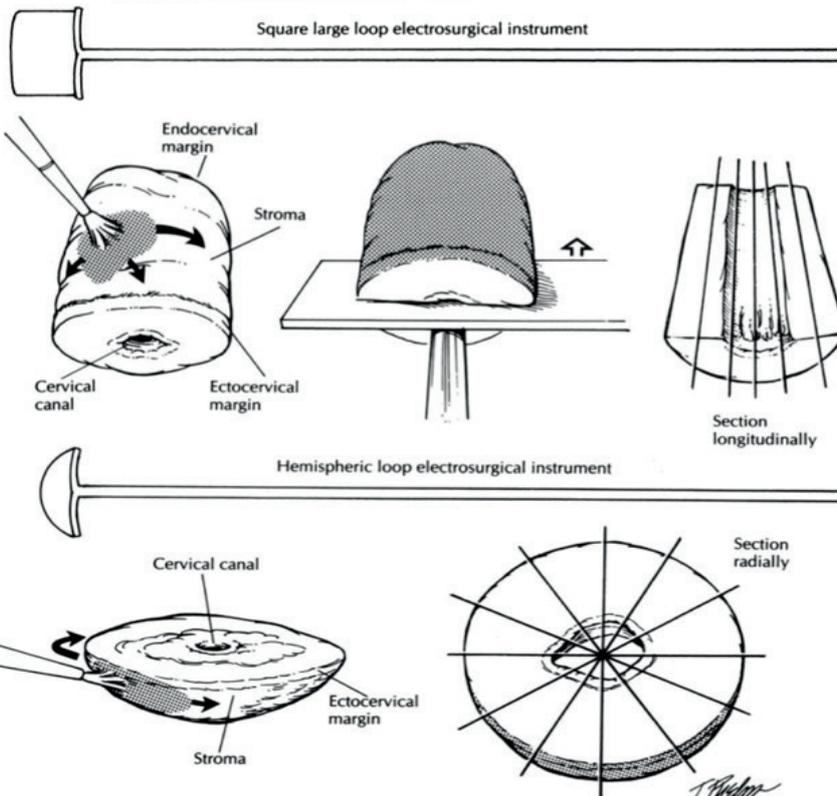
Radical Hysterectomy for Cervical Cancer

1. Orient the uterus: The round ligaments are most anterior, and the ovaries, if present, are most posterior. The peritoneum extends further inferiorly along the posterior uterus than it does anteriorly.
2. Apply ink as shown.
3. Remove the bilateral parametrial/paracervical tissues, and section them separately at 0.3-cm intervals.
4. Amputate the cervix, and open it like a cone biopsy. Section the entire cervix longitudinally at 0.3-cm intervals. Document the size and depth of invasion of the tumor.
5. Shave the vaginal cuff margin.
6. Take a transverse section of the lower uterine segment, then bivalve the uterine corpus and bread-loaf it at 0.5-cm intervals.
7. Submit full-thickness sections of tumor and one section of each uninvolved cervical quadrant. Include vaginal margins, anterior and posterior soft tissue margins, right and left parametrial/paracervical tissues in their entirety, transverse sections of the upper endocervix and lower uterine segment, and standard sections of anterior and posterior endomyometrium.



Loop Electrocautery Excisions of the Cervix

1. Orient the specimen by identifying the ectocervical and endocervical margins.
2. Ink the endocervical margin and the stromal/ectocervical margins with separate colors.
3. For small cylindrical specimens, divide in half and section longitudinally.
4. For shallow, saucer-shaped specimens, section radially—like a pie.
5. Submit the entire specimen.





B: ENDOMETRIUM

Introduction

Risk of endometrial cancer is related to increasing age, late menopause, never giving birth, infertility, obesity, diabetes, high blood pressure, estrogen treatment, or tamoxifen therapy. Women with hereditary non-polyposis colon cancer (HNPCC)/Lynch syndrome have a very high risk of endometrial cancer.

The most common presenting symptom is abnormal uterine bleeding. Other symptoms are pain, weight loss and abdominal mass. Diagnosis is made by way of endometrial biopsy for histology examination. Endometrial biopsy may involve taking a sample from the cervix as well, called fractional curettage. Ultrasound examination to assess the endometrial cavity can also be helpful. The treatment modalities of confirmed cancer are surgery, chemotherapy, radiotherapy and hormonal therapy. Endometrial carcinoma may share histologic features with ovarian carcinoma.

Specimen types

1. Curettings/pipelle biopsy
2. Hysterectomy

	Personnel	Indication	Fixation	Facilities
Curettings	Gynaecologist/ medical officers	Diagnosis	Fix immediately	Level IV, V, VI
Hysterectomy	Gynaecologist	Treatment	Fix immediately	Level IV, V, VI

Specimen handling

1. Curetting & pipelle biopsy-

- A. Sample is immediately fixed in 10% NBF and submitted to the laboratory accompanied by duly filled requisition form
- B. Allow fixation for a minimum of 6 hours
- C. Sample is grossed – Number, size(s), colour and general appearance
- D. All the sample is Processed, embedded, sectioned and stained as per SOPs
- E. Examination and Reporting
- F. dispatch of results to requesting clinician

2. Uterus

Uterus is removed as part of surgical treatment of endometrial cancer diagnosed through either curettings or pipelle biopsies. Proper handling of this sample is essential for confirmation of the diagnosis, determination of the grade and stage of the cancer to enable optimal care.

GROSSING HYSTERECTOMY SPECIMENS-

1. The specimen is fixed in 10% BNF for a minimum of 6 hours.
2. Orient, weigh, and ink the soft tissue resection margins around the cervical canal.
3. Ink the parametrial tissue, which extends along the body of the uterus and into the broad ligament.
4. If the adnexa are present, remove them at their lateral insertions along the uterus.
5. Make multiple transverse cuts through the ovary and fallopian tube, looking for evidence of either direct tumour extension or metastatic spread. Submit at least one section from each side to demonstrate the ovary and fallopian tube with adjacent soft tissue.
6. Bivalve the uterus by using a long, sharp knife guided by a probe placed through the cervical canal. Closely examine

the endometrial cavity and describe the findings. While the tumour is fresh, remove a portion to freeze for future molecular diagnostic tests if desired. The bivalved uterus may now be photographed.

7. The dissection begins with longitudinal sectioning of the cervix. Extend these incisions to the lower uterine segment to include both endometrial and endocervical mucosal surfaces.
8. Note whether or not the tumour grossly involves the endocervical mucosa and/or stroma. Submit a section of this region from the anterior and posterior halves to evaluate for tumour extension into the cervix, an important factor in determining the stage of the cancer.
9. Serially bread-loaf the uterine corpus and lower uterine segment with transverse sections. Record the size, location, and appearance of the tumour.
10. Describe the pattern of invasion. Does the tumour have a broad pushing front, an infiltrating finger-like pattern, or is it discontinuous?
11. Measure the greatest depth of tumour invasion into the myometrium starting from the normal junction of the endometrium and the myometrium. In addition, measure the total myometrial thickness at this point, and specify the uninvolved distance from the deep tumour/myometrial junction to the serosa.
12. When selecting sections for histologic analysis, include the deepest point of tumour invasion as well as the interface with grossly uninvolved endometrium.
13. The best sections are those that show the full thickness from the endometrium to the serosa. Sometimes, however, the myometrium may be too thick to fit in a standard-size tissue cassette. In these situations, divide the section into endometrial and serosal halves. Designate their relationship clearly in your summary of sections.
14. Lymph nodes from the pelvic and para-aortic regions may also be included as separate specimens.

Minimum reporting items in the surgical report

1. Procedure and what structures/organs are present.
2. Tumour size.
3. Histologic type and grade of neoplasm.
4. Maximum depth of tumour invasion (in millimeters)- Measured from the normal endometrial/myometrial junction.
5. Myometrial thickness at the deepest point of invasion (in millimeters).
6. Distance from the deepest tumour/ myometrial junction to the serosa (in millimeters).
7. Whether tumour extend through the serosa.
8. Involvement of endocervix. (Specify surface glandular and/or stromal involvement.)
9. Lymphovascular space invasion seen.
10. Adnexa involvement.
11. Lymph node involvement
12. Margins (cervical/vaginal, right paracervical/parametrial, left paracervical/parametrial). Distance of the tumour from closest margin (in centimeters).
13. Lymph nodes involvement (Include the number of nodes involved and the number of nodes examined at each specified site.)

References

1. National Cancer Screening Guidelines – Kenya
2. AJCC Cancer Staging Atlas (2006) Surgical pathology illustrated guide.
3. College of American Pathologists cancer reporting tools (<https://www.cap.org> › Protocols and Guidelines › Cancer Reporting Tools)

C: OVARY

Ovarian cancer is the sixth most common cancer in women and the seventh most common cause of cancer death. More than 90% of primary ovarian cancers are of epithelial origin. The other types are Germ cell tumours, Sex cord stromal tumours, lymphoproliferative neoplasm and secondary (metastatic) lesions especially from the GIT.

Ovarian cancer presence as pelvic discomfort, pelvic or lower abdominal mass and ascites. When suspected, the patient undergoes a laparotomy followed by removal of the ovarian mass with or without the removal of the uterus and ovary/tube. Special considerations should be put to the proper handling of ovarian tumour specimens to ensure that all the diagnostic and prognostic data are captured

Ovarian cystectomy	Removal of the cyst only (Mostly for benign tumours)	MO/Surgeon/ Gynaecologist	Level IV, V, VI
Oophorectomy	Removal of ovary with tumour (Can be unilateral or bilateral)	Gynaecologist	Level IV, V, VI
Salpingo-oophorectomy	Removal of ovaries and the attached fallopian tubes.	Gynaecologist	Level IV, V, VI
Hysterectomy and salpingo-oophorectomy	Removal of ovaries together with uterus and fallopian tubes	Gynaecologist	Level IV, V, VI
Oophorectomy and omentectomy	Removal of ovaries and omentum	Gynaecologist	Level IV, V, VI

Handling

The specimen is fixed in 10% neutral buffered formalin

Gross Description

- Document the weight and dimensions of the specimen. Also describe and measure the other structures included (Uterus, fallopian tube, omentum)
- Examine the surface for evidence of rupture, adhesions, or nodular tumour excrescences. If present, these are inked for orientation.
- Section the ovarian mass at 1-cm intervals through its longest axis
- Document the colour and consistency of the cyst fluid (serous, mucinous, or haemorrhagic)
- Document whether the mass is solid, cystic, or both (document the percentage of each region)

- Examine the surfaces of the cysts for evidence of granularity, nodules, or papillary projections. Record the thickness of the cyst walls
- Describe any regions of haemorrhage or necrosis. Try to find any residual ovarian parenchyma. (Mostly in the region immediately adjacent to the fallopian tube.)
- Submit the tumour sections- from solid, haemorrhagic or necrotic regions- with a minimum of one section per 1 to 2 cm of the greatest tumour dimension. (If the tumour is uniform throughout, fewer sections may be prudent.)
- Cysts that show granular, nodular, or papillary excrescences should be thoroughly sampled.
- Omentectomy specimens should be weighed, measured, and serially sectioned at 0.5-cm intervals to look for gross tumour nodules. Measure the size of the gross tumour and specifically indicate if it is 2 cm or less or more than 2 cm for staging purposes.



Summary of Data set for reporting Ovarian Carcinoma

The request form should provide:

- Patient's demographics
- Prior chemotherapy
- Specimen type
- Previous cytology/biopsy results
- Capsule status at surgery
- Previous tumor markers where applicable

Macroscopic examination

- Specimen visual appearance and consistency as submitted and the dissection surface
- Capsule status
- Tumor site and size
- Dimensions of omentum if submitted
- Size of maximum omental deposits if present
- Number and sizes of other tissues submitted with the ovary

Microscopy

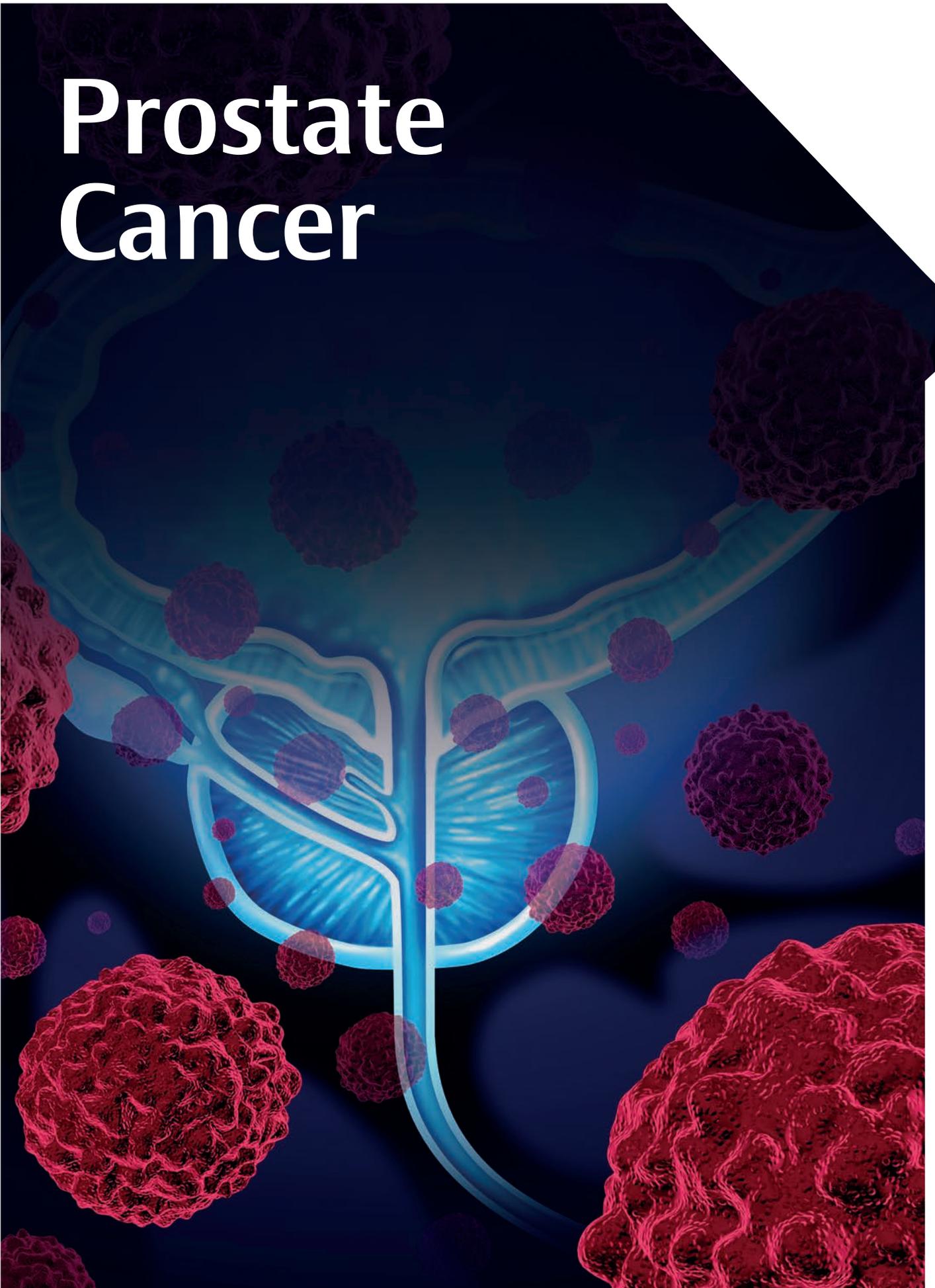
- Tumor type
- Grade
- Sites of involvement
- Peritoneal cytology
- Lymph node status
- Provision of FIGO/TNM staging
- For borderline tumors, provide micropapillary architecture and presence of implants

Please find use this link to access the complete data set for Ovarian Cancer reporting:
www.rcpath.org

References

- a. CAP Guidelines 2018

Prostate Cancer





Introduction

Proper handling of the prostatic specimen is extremely crucial for an accurate diagnosis, hence the importance of a clinician’s manual to provide guidance. There is need for multidisciplinary sensitization and training in prostatic specimen procurement, handling and reporting as this greatly impacts on the usefulness of the final pathology report.

Sampling institutions are encouraged to develop a clinician manual to address aspects of prostate biopsies with regard to quality, adequacy, preservation, and transport to the laboratory.

Specimen type/procedures

- **Needle Biopsy**- This should be performed by the urologist, general surgeon, intervention radiologist or a medical officer trained in this procedure. The procedure can be done either under image or finger guidance and should be 6 to 12 cores of at least 1cm in length each.
- **Transurethral Prostatic Resection (TURP)**- This should be performed by the urologist, general surgeon trained in this procedure.
- **Suprapubic or Retropubic Enucleation (Subtotal Prostatectomy)** - This should be performed by the urologist, general surgeon trained in this procedure.
- **Radical Prostatectomy** - This should be performed by the urologist.

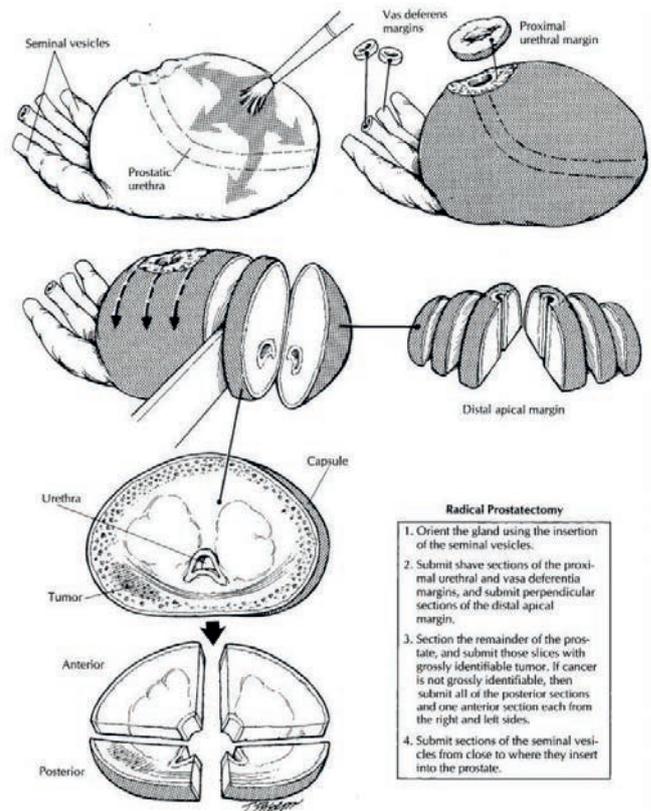
Specimen handling and sampling.

All specimens should immediately be fixed in 10% neutral buffered formalin for a minimum of 6 hours in sufficient volumes of fixative (10 times or more of the sample).

- **Needle biopsies**
All cores should be sampled and submitted as two cores per cassette. The number and length in millimetres (longest and shortest) should be indicated in the request form.
- **TURP/Enucleation**
Specimens that weigh 12 g or less should be sampled in their entirety in 6 to 8 cassettes while for those more than 12g the initial 12 g (15GM) are submitted (6 to 8 cassettes), and 1 cassette may be submitted for every additional 5g may be submitted. In case of incidental malignancy, the entire specimen should be sampled.
- **Radical Prostatectomy**
This specimen should include the prostate, seminal vesicles, prostatic urethra, bladder neck and lymph nodes.

The surgeon should orient the specimen by labelling the margins.

In the laboratory, the margins should be painted or otherwise marked. The specimen may be sampled in its entirety or partially sampled in a systematic fashion. This should be done in line with the attached protocol. The image below shows a radical prostatectomy specimen and how it should be grossed.



Report

The Pathology reports will be in line with the protocols modified from the CAP protocols. In summary, all reports will provide the following:

a. NEEDLE BIOPSY reports should include:

- Patient identifiers and clinical information
- Specimen description including number of cores and dimensions in cm
- Qualities of the biopsy
- Tumour histologic type
- Intraductal carcinoma
- Tumour quantity (in mm or percentage)
- Tumour grade (gleason score and isup\who\ grade group\ cap guidelines)
- Lymphovascular invasion
- Periprostatic fat invasion
- Perineural invasion
- Pre - treatment effects
- Other pathological processes.

b. TURP/ENUCLEATION biopsies positive for malignancy should include:

- Patient identifiers and clinical information
- Specimen description including weight and dimensions in centimetres

Qualities of the biopsy

- Tumour histologic type
- Tumour quantity (estimate % of turp chips involved by tumour\size of tumour in mm in enucleation)
- Tumor grade (gleason score and isup\who\ grade group\cap guidelines)
- Lymphovascular invasion periprostatic fat invasion perineural invasion
- Treatment effects (radiation\hormonal\other therapy effects)
- Other pathological processes.

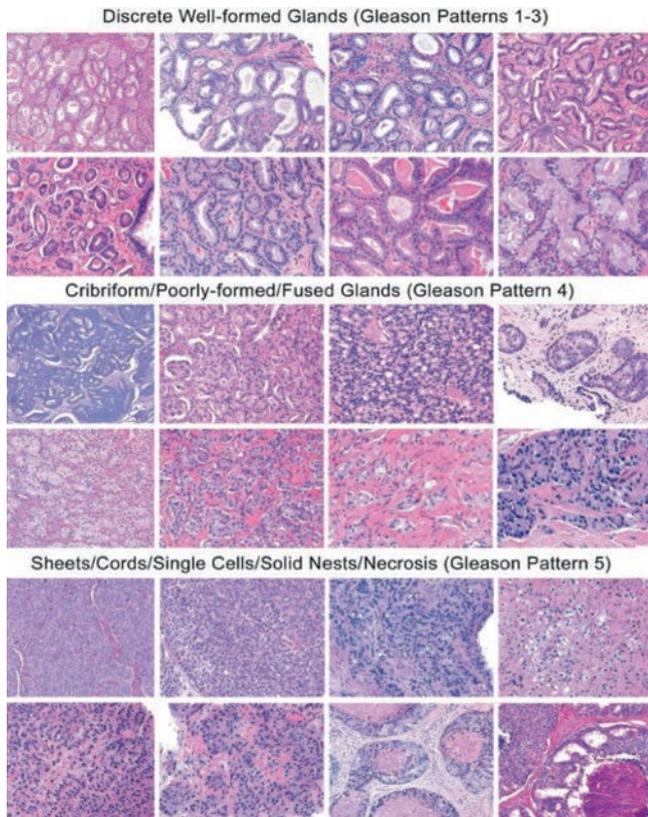
c. Radical Prostatectomy reports should include:

- Patient identifiers and clinical information
- Specimen description as per grossing protocol see appendix
- Tumour histologic type
- Tumour quantity
- Tumour grade (gleason score and isup grade\who\grade group)
- Lymphovascular invasion periprostatic fat invasion perineural invasion
- Urinary bladder neck invasion
- Seminal vesicle invasion (invasion of muscular wall required)

Margins

- Regional lymph nodes. (Number of lymph nodes submitted. Number of lymph nodes involved. Extranodal extension
- Pathologic tumour stage\ptmn treatment effects
- Other pathological processes

The images below show the microscopic description of the Gleason Pattern Scoring system for cancer of the prostate



The table below shows the current WHO/ISUP grade groups for cancer of the prostate

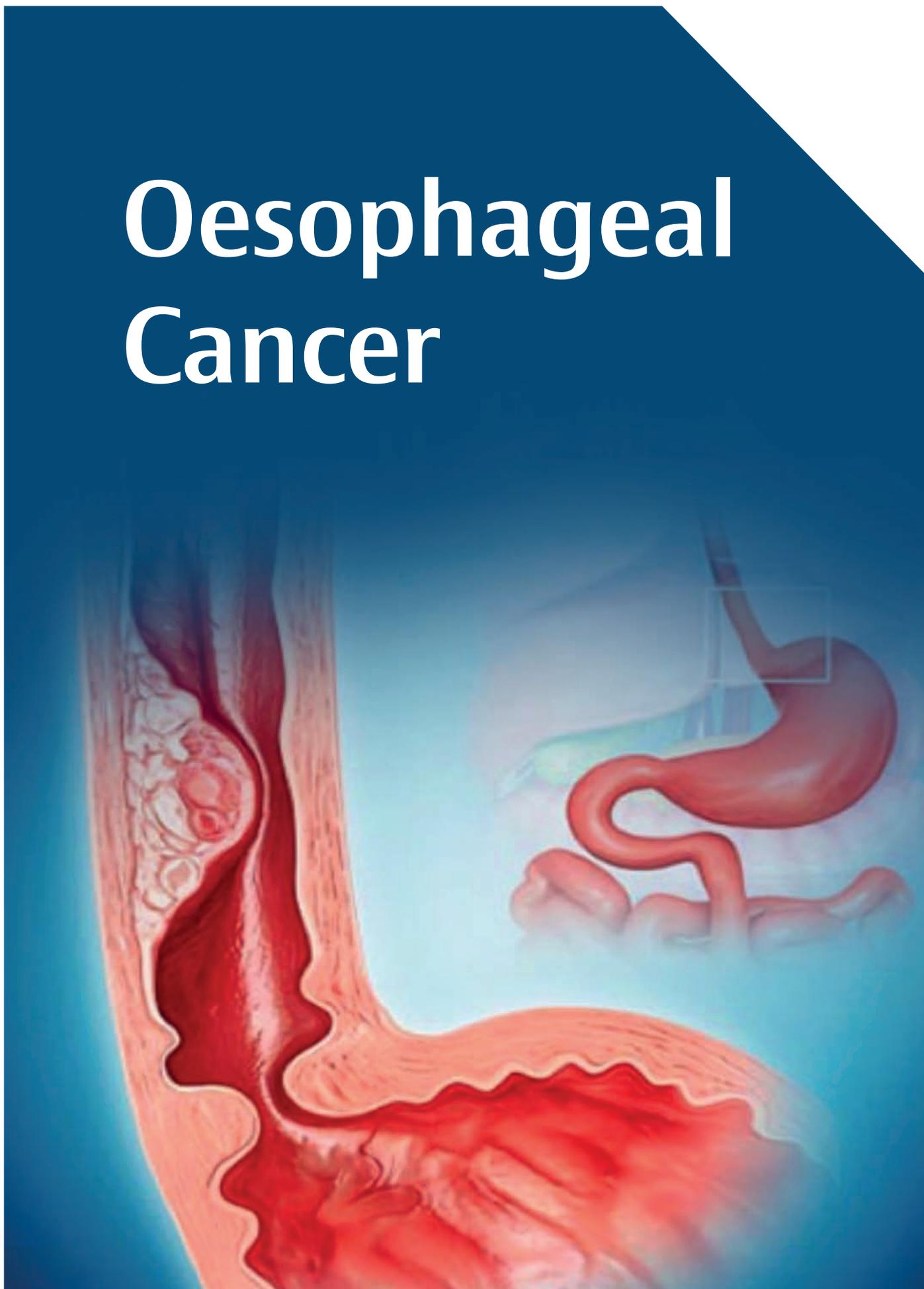
ISUP grade group	Gleason score	Charadertstlcs
Grade group 1	3+3 =6	Hlstromorphologlclly made up of distinct well delimited glandular ducts.
Grade group 2	3+4 =7	Hlstromorphologlclly prlnclpally made up of dlstlnct glands with minor constituent of defectvely shaped, merged or cribriform glandular ducts.
Grade group 3	4+3 =7	Hlstromorphologlclly princpally made up of defectvely shaped, merged or cribriform glandular ducts with minor constituent of distinct glands.
Grade group 4	4+4 or 3+5 or 5+3 = 8	Hlstromorphologlclly princpally made up of defectvely shaped, merged or cribriform glandular ducts or princpally a mix distinct glands and no glandular formation.
Grade group 5	9-10	Hlstromorphologlclly tumor lacks glandular formation (or necrotic glands) with or devoid of defectvely shaped.

References

1. CAP Guidelines 2018
2. WHO/ISUP group grading for prostate cancer



Oesophageal Cancer



Introduction

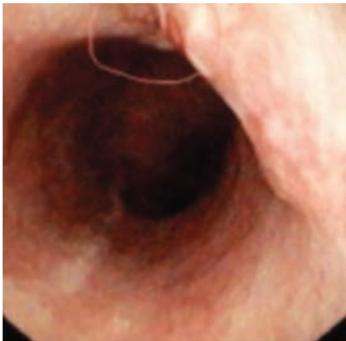
Esophageal cancer is a leading cause of death in both sexes in Kenya, has poor prognosis when presenting late. It has a long pre-invasive period when diagnosis can be made from early endoscopy and biopsy. Pre-cancerous states have similar progression as other squamous intraepithelial lesions and are amenable to cytologic evaluation. Patients frequently present late for endoscopy, but have frequently been treated for variable periods prior, in health facilities, where clinical suspicion was low.

Endoscopic specimens are generally small. Optimal handling is required to avoid a partial or complete loss of specimen at processing.

Esophageal brush or wash cytology specimens are possible, but not frequently performed in our health setting early esophageal cancer diagnosis shall improve the prognosis and, and reduce morbidity and mortality.

Diagnostic Workup

- Detailed history and physical examination: Dysphagia, odynophagia, hoarseness, weight loss, use of tobacco, nitrosamines, history of GERD. Examine for cervical or supraclavicular adenopathy.
- Confirmation of diagnosis:
 - EGD: allow direct visualization and biopsy, measure proximal & distal distance of tumor from incisor, presence of Barrett's esophagus.



Early, Superficial cancer



Circumferential ulceration esophageal cancer



Malignant stricture of esophagus

Grossing Procedure

1. Record the location of the tumour in the esophagus (cervical, upper thoracic, middle thoracic, lower thoracic, abdominal) with respect to the macroscopic esophageal gastric junction (EGJ) (defined as where the tubular esophagus meets the stomach, as measured from the top of the gastric folds).
2. Record the maximum longitudinal and transverse dimension of the tumour mass, the distance of the tumour midpoint from the EGJ, and the relative proportions of the tumour mass located in the esophagus and in the stomach.
3. Paint the circumferential surface, proximal and distal margins of the specimen to assist in evaluation of margin status. 21`
4. Sample the tumor ensuring that the tumour is sampled at point of maximal invasion, distal, proximal and radial margins, surrounding esophagus and any other lesion of interest.

Endoscopic biopsies

Biopsies shall be 4-6mm in aggregate and be representative of the Lesion. This requires proper correlation with endoscopic, clinical and imaging findings

Specimen handling

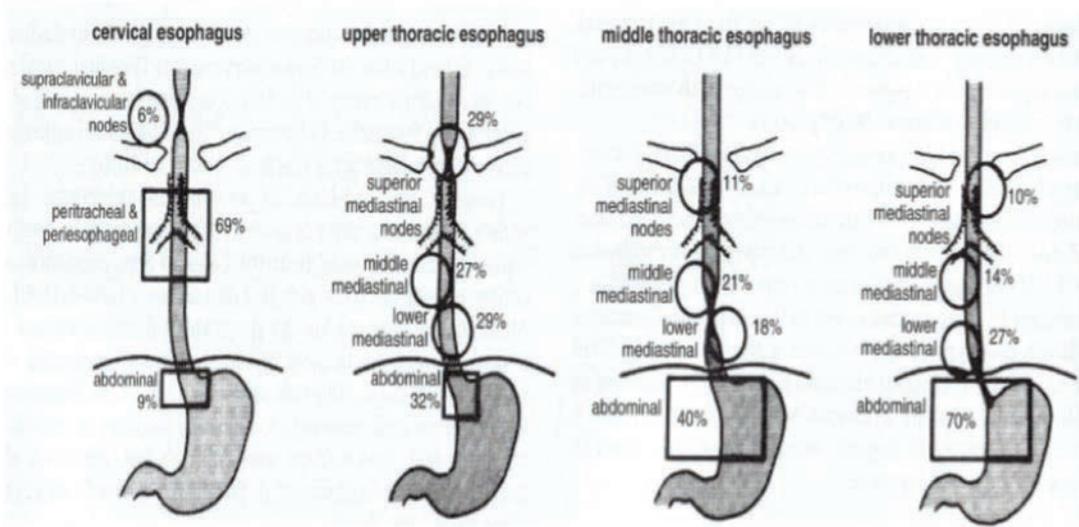
The specimen will be fixed in 10% neutral buffered formalin for a minimum of six hours.

- Endoscopic biopsy will be processed in its entirety.
5. Measure the distance from the tumour edge to the closest resection margin(s) if all margins are uninvolved by invasive carcinoma.
 6. Proximal and distal resection margins should be evaluated for Barrett's esophagus and for squamous and glandular dysplasia if they are not involved by invasive carcinoma.
 7. All lymph nodes submitted should be sampled and counted

Type of specimen	source
Endoscopic biopsy	Gastroenterologist, surgeon, or trained medical officer
Resection specimen (esophagectomy/ Esophagogastrectomy)	Surgeon/ cardiothoracic surgeon



Site-wise nodal involvement



Protocol for the Examination of Resection Specimens from Patients with Carcinoma of the Oesophagus (MINIMUM DATA SET)

- Tumour Site (select all that apply)
- Relationship of Tumour to Esophagogastric Junction
- Tumour Size
- Histologic Type
- Histologic Grade (required only if applicable) Tumour Extension
- Margins
- Response to Previous therapy
- Response of tumour to previous chemotherapy or radiation therapy should be reported using the modified Ryan Scheme

Modified Ryan Scheme for Tumour Regression Score¹¹

Description	Tumour Regression Score
No viable cancer cells (complete response)	0
Single cells or rare small groups of cancer cells (near complete response)	1
Residual cancer with evident tumour regression, but more than single cells or rare small groups of cancer cells (partial response)	2
Extensive residual cancer with no evident tumour regression (poor or no response)	3

Prognostic/Stage Groupings

Different stage groupings are used for squamous cell carcinomas and adenocarcinomas. In addition, a separate stage grouping is used to stage patients receiving neoadjuvant treatment due to the fact that prognostic implication for ypTNM differs from those of equivalent pTNM.

Location plays a role in the stage grouping of oesophageal squamous cell carcinomas:

Location Category	Location Criteria
X	Location Unknown
Upper	Cervical oesophagus to lower border of azygos vein
Middle	Lower border of azygos vein to lower border of inferior pulmonary vein
Lower	Lower border of inferior pulmonary vein to stomach, including gastroesophageal junction
Note: Location is defined by the position of the epicenter of the tumour in the o.	

Stage Groupings: Squamous Cell Carcinoma. See CAP/Other current links

Stage Grouping: Adenocarcinoma

Stage T N M G

Stage grouping: ypTNM (applies to both squamous and adenocarcinomas)

Stage T N M

Ancillary testing: MSI and HER2 overexpression:

These can be done for patients with locally advanced or recurrent or metastatic adenocarcinoma for whom Trastuzumab is being considered, or in patients who are candidates for treatment with PD1 inhibitors.

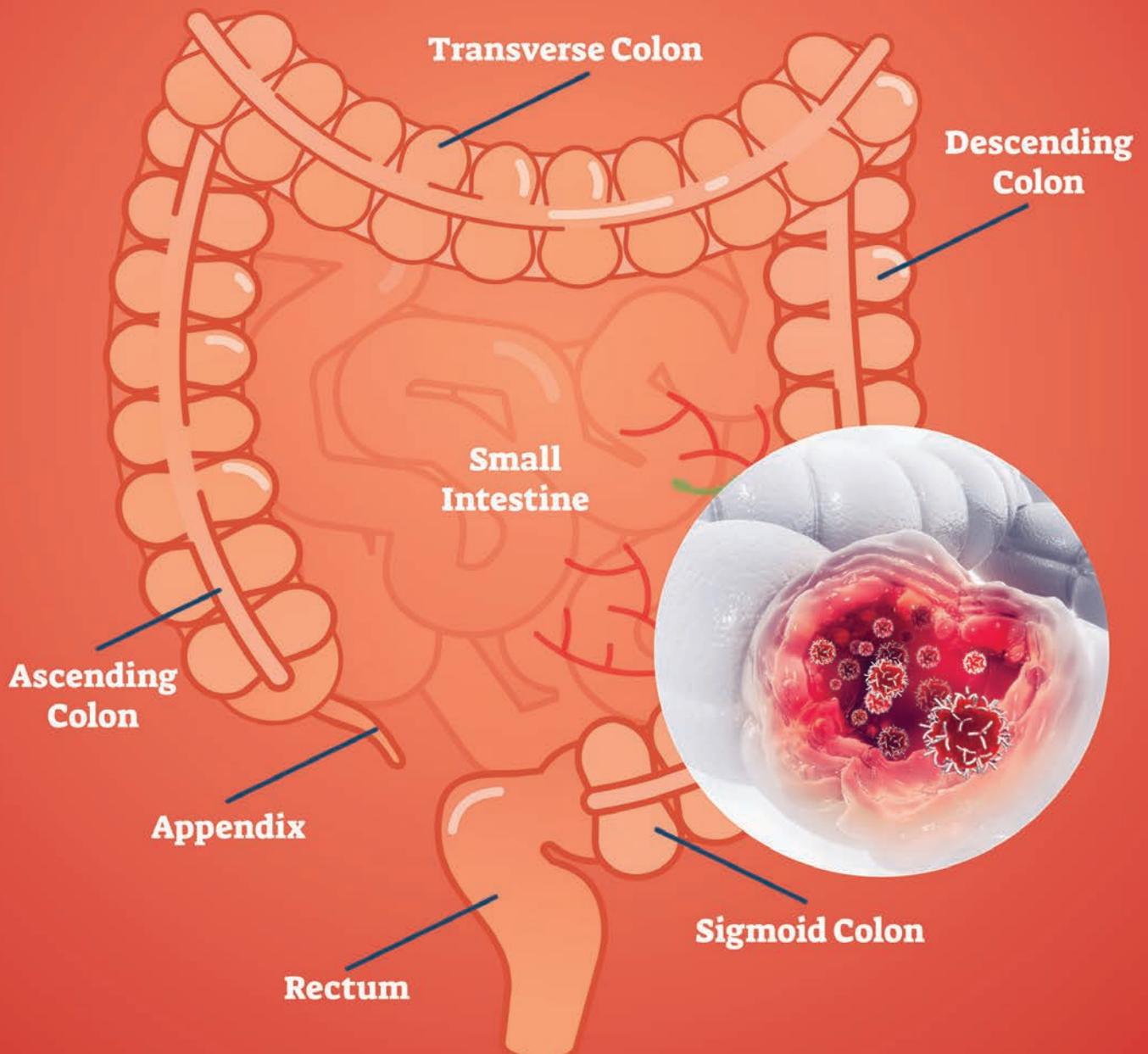
References

CAP Cancer Protocols 2018

8th Edition, AJCC Staging Manual

Ryan R, Gibbons D, Hyland JM, et al. Pathological response following long-course neoadjuvant chemoradiotherapy for locally advanced rectal cancer. *Histopathology*. 2005;47(2):141-146

Colorectal Cancer





Introduction

Screening for colon cancer has different modalities as outlined in the National cancer screening guidelines (2019). Mainstay for diagnosis is colonoscopy with biopsy / polypectomy. Colonoscopy must be on a fully prepared bowel to allow adequate visualization of the entire large bowel for purpose of assessing synchronous and metachronous lesions.

During colonoscopy, the lesion must be fully described in terms of number site/distance from the anal verge and nature (ulcerated, haemorrhagic, fungating or polypoid). For more than one lesion, biopsy should be submitted separately and clearly labelled as to the site. Penduculated lesions should be fully excised (total polypectomy). Adequate sampling for punch biopsies should be

performed (6-8 fragments). The specimen should be immediately and fully submerged in fixative. Patients diagnosed with cancer should have a staging modality done which includes a chest x-ray and abdomino-pelvic CT scan prior to surgery. All cases must be presented and discussed in a multidisciplinary tumor board at the institution or teleconference for adequate treatment planning. Locally advanced and metastatic disease with no complication of bleeding or obstruction may be amenable to neoadjuvant chemo radiotherapy. Surgery may be for curative or palliative intent. Curative colon surgery must include adequate lymphnode harvest and negative margins. The resection specimens should be submitted as a whole to the laboratory fully immersed in formalin ratio 1:10.

	Personnel	Indication	Fixation	FACILITYs
Polypectomy	Surgeon /gastroenterologist	Diagnosis / treatment	Fix immediately	Level IV,V,VI
Endoscopic punch biopsy	Surgeon /gastroenterologist	diagnosis	Fix immediately	Level IV,V,VI
Resection	Surgeon	Treatment / staging	Fix immediately	Level V,VI,

Specimen types

1. Polypectomy
2. Endoscopic punch biopsy
3. Resection

Specimen handling

1. Punch biopsy- processes all.
2. Polypectomy – ink stalk margins and process the entire specimen
3. Resection specimens

The specimen should be left in formalin for a minimum of six hours before grossing. During grossing describe the size of the specimen, the site of the tumour and resection margins. Specimen should be processed according to attached protocol (appendix)

GROSSING COLORECTAL RESECTION SPECIMENS

1. Specify the site of tumour - the right (cecum, ascending), transverse, left or sigmoid colon, rectum or small intestine.
2. Tumors within the non- distal portion and by definition all tumors within 16cm of the anal verge are rectal. For rectal tumors, the location of the tumor is relative to peritoneal reflection.
3. When present the radial margin should be inked fresh. For rectal tumors, ink the soft tissue margin beneath palpable tumor.
4. Open specimen longitudinally with scissors. Avoid cutting through the tumor by using your index finger placed inside the lumen to palpate for the tumor.
5. Identify all mesenteric nodes. Divide nodes into those subjacent to the tumor, proximal to tumor and distal to tumor. If a mesenteric apex can be identified, submit nodes from it separately. All grossly negative lymph nodes should

be submitted entirely. If fewer than 12 lymph nodes are identified, a second search should be made. If available, fat may be post-fixed in Bouin’s solution to facilitate the process.

6. Site within colorectum. In the case of rectal cancer, state the distance of the most distal point of the anterior peritoneal reflection from the distal margin and the length of the tumor above and below the reflection. State, if possible, the quadrant showing the site of deepest tumor invasion (anterior, right lateral, posterior, and left lateral) and estimate the proportion of the circumference that is involved (multiples of 10%).
7. Appearance of mesorectal excision in the case of rectal cancer (complete when invested by shiny fascia and with only minor breaches)
8. Tumor: size, distance from margins, exophytic, ulcerated, colour, depth of invasion. Submit at least 3 sections from the tumor, including tumor/normal mucosa interface and the deepest point of penetration.
9. Non-tumoral mucosa and bowel wall appearance. Submit polyps and all unusual areas.
10. Labels blocks e.g. A1 -Proximal margin (specify as perpendicular or circumferential; circumferential preferred if tumor is located within 20 mm of the margin), A2- Distal margin (specify as perpendicular or circumferential; circumferential preferred if tumor is located within 20 mm of the margin) A3-5 Tumor A6 Non-neoplastic mucosa A7 Lymph nodes

Minimum reporting items in the surgical report

1. Excisional Biopsy (Polypectomy)

- Tumor Site (Caecum, sigmoid etc.)
- Specimen Integrity (Intact, fragmented)
- Polyp Size
- Polyp Configuration (Pedunculated with stalk, Stalk length, Sessile)
- Size of Invasive Carcinoma
- Histologic Type (mucinous, signet ring etc.)
- Histologic Grade (differentiation)
- Tumor Extension- invasion to the wall
- Margins Deep Margin (Stalk Margin), Mucosal Margin (required only if applicable)
- Lymphovascular Invasion (select all that apply)
- Type of polyp in which invasive carcinoma arose (tubular, villous etc.)

2. Resection

- Procedure (right hemicolectomy, sigmoidectomy, etc.)
- Tumor Site (cecum, T=transverse colon, etc.)
- Tumor Location- entirely above the anterior peritoneal reflection, entirely below the anterior peritoneal reflection or straddles the anterior peritoneal reflection
- Tumor Size

- Macroscopic Tumor Perforation
- Macroscopic Intactness of Mesorectum (if applicable) – complete, nearcomplete, incomplete
- Histologic Type-adenocarcinoma, mucinousadenocarcinoma
- Histologic Grade
- Tumor Extension- to the wall or adjacent organs
- Margins (proximal margin, distal margin, radial or mesenteric margin)
- Lymphovascular Invasion
- Perineural Invasion
- Type of Polyp in Which Invasive Carcinoma Arose
- Tumor Deposits
- Regional Lymph Node
 - number of lymph nodes submitted or found
 - number of lymph nodes involved:
 - number of lymph nodes examined
- Pathologic Stage Classification (pTNM, AJCC 8th Edition)
 - TNM Descriptors (multiple primary tumors, recurrent, posttreatment)
 - Primary Tumor (pT)
 - Regional Lymph Nodes (pN)
 - Distant Metastasis (pM) (required only if confirmed pathologically in this case)
- Ancillary Studies (K-Rras, EGFR, MSI)

Protocol for the Examination of Specimens from Patients with Primary Carcinoma of the Colon and Rectum (resection)

Description	
Colectomy	Includes specimens designated total, partial, or segmental resection
Rectal Resection	Includes specimens designated low anterior resection or abdominoperineal resection
Tumor Type	Description
Carcinoma	Invasive carcinomas including small cell and large cell (poorly differentiated) neuroendocrine carcinoma

- **Select a single response unless otherwise indicated.**

• Procedure

___ Right hemicolectomy__Transverse colectomy__Left hemicolectomy__Sigmoidectomy__Low anterior resection etc

• Tumor Site (select all that apply)

• ___ Cecum__Ileocecal valve__Right (ascending) colon__Hepatic flexure__Transverse colon__ Splenic flexure__Left (descending) colon etc

• Tumor Location (applicable only to rectal primaries)

• -Entirely above the anterior peritoneal reflection__Entirely below the anterior peritoneal reflection__Straddles the anterior peritoneal reflection__Not specified

• Tumor Size

• Three dimensions

• Macroscopic Tumor Perforation

• Not identified__Present__ Cannot be determined

• Macroscopic Intactness of Mesorectum (if applicable)

• ___ Complete ___ Near complete___ Incomplete ___ Cannot be determined

• Histologic Type

• ___ Adenocarcinoma__Mucinous adenocarcinoma___ Signet-ring cell carcinoma

• ___ Medullary carcinoma

• Histologic Grade

• ___ G1: Well differentiated ___ G2: Moderately differentiated___ G3: Poorly differentiated___ G4: Undifferentiated

• Tumor Extension

• Margins

___ All margins are uninvolved by invasive carcinoma, high-grade dysplasia, intramucosal adenocarcinoma, and adenoma
Margins examined: _____

+ Distance of invasive carcinoma from closest margin (millimetresorcentimetres): ___ mm or ___ cm

+ Specify closest margin: _____

Distance of tumor from radial margin (required only for rectal tumors) (millimetresorcentimetres):

___ mm or ___ cm

+ Distance of tumor from distal margin (recommended for rectal tumors) (millimetresorcentimetres):

___ mm or ___ cm



Individual margin reporting required if any margins are involved or margin involvement cannot be assessed

- Proximal Margin**

Cannot be assessed Uninvolved by invasive carcinoma (Distance of tumor from margin) Involved by invasive carcinoma

- Distal Margin**

Cannot be assessed Uninvolved by invasive carcinoma (Distance of tumor from margin) Involved by invasive carcinoma

- Radial or Mesenteric Margin**

Cannot be assessed Uninvolved by invasive carcinoma (Distance of tumor from margin) Involved by invasive carcinoma

- Deep Margin**

Cannot be assessed
 Uninvolved by invasive carcinoma
 + Distance of tumor from margin (millimetres/centimetres): mm or cm
 Involved by invasive carcinoma

Treatment Effect

- No known presurgical therapy
- Present (No viable cancer cells (complete response, score 0), Single cells or rare small groups of cancer cells, Residual cancer with evident tumor regression, but more than single cells or rare small groups of cancer cells, absent)
- Lymph-vascular Invasion (select all that apply)
- Perineural Invasion
- Type of Polyp in Which Invasive Carcinoma Arose
- None identified, Tubular adenoma, Villous adenoma, Tubulovillous adenoma etc
- Tumor Deposits
- Not identified, Present (Specify number of deposits), Cannot be determined
- Regional Lymph Nodes**
- No lymph nodes submitted or found
- Number of Lymph Nodes Involved: , Number of Lymph Nodes Examined:
- Pathologic Stage Classification (pTNM, AJCC 8th Edition)
- TNM Descriptors (required only if applicable) (select all that apply)
- m (multiple primary tumors), r (recurrent), y (posttreatment)

Primary Tumor (pT)

pTX: Primary tumor cannot be assessed
 pT0: No evidence of primary tumor

- pT1: Tumor invades the submucosa (through the muscularis mucosa but not into the muscularis propria)
- pT2: Tumor invades the muscularis propria
- pT3: Tumor invades through the muscularis propria into pericolorectal tissues
- pT4: Tumor invades the visceral peritoneum or invades or adheres to adjacent organ or structure

Regional Lymph Nodes (pN)

- pNX: Regional lymph nodes cannot be assessed
- pN0: No regional lymph node metastasis
- pN1: One to three regional lymph nodes are positive (tumor in lymph nodes measuring ≥ 0.2 mm), or any number of tumor deposits are present and all identifiable lymph nodes are negative
- pN2: Four or more regional lymph nodes are positive

Distant Metastasis (pM) (required only if confirmed pathologically in this case)

- pM1: Metastasis to one or more distant sites or organs or peritoneal metastasis is identified
- pM1a: Metastasis to one site or organ is identified without peritoneal metastasis
- pM1b: Metastasis to two or more sites or organs is identified without peritoneal metastasis
- pM1c: Metastasis to the peritoneal surface is identified alone or with other site or organ metastases

Additional Pathologic Findings (select all that apply)

None identified, Adenoma(s), Ulcerative colitis etc

Ancillary Studies

Microsatellite Instability (MSI) Testing
 MSI-high (>30%), MSI-low (10-30%), MSI-stable (0%)



Figure 1. A, Mesenteric margin in portion of colon completely encased by peritoneum (dotted line). B, Circumferential margin (dotted line) in portion of colon incompletely encased by peritoneum. C, Circumferential margin (dotted line) in rectum, completely unencased by peritoneum.

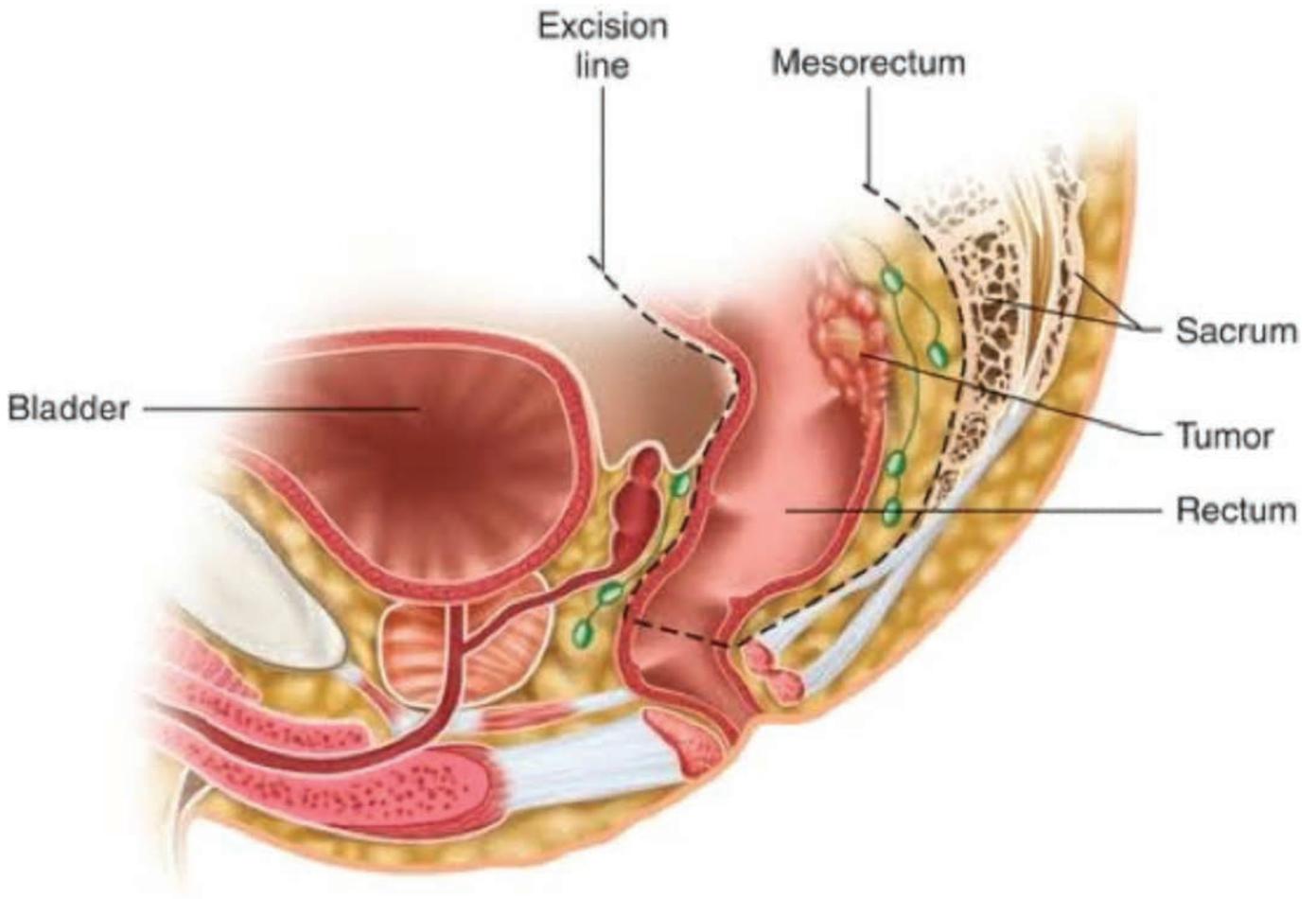


Figure 2. Total Mesorectum resection.

References

1. National Cancer Screening Guidelines – Kenya
2. AJCC Cancer Staging Atlas (2017)
3. College of American Pathologists cancer reporting tools (<https://www.cap.org> > Protocols and Guidelines > Cancer Reporting Tools)



Childhood Cancers

Introduction

According to World Health Organization (WHO), a child is defined to be 19 years or younger. Globally, the annual incidence of cancer in children is estimated at 300,000 cases (GLOBOCAN, 2018). Genetic factors, environmental factors such as ionizing radiation, chemicals and infectious agents have also been linked to cancer causation. Common childhood neoplasm cancers in Kenya are Leukemia, Lymphoma (Burkitt's, Hodgkin's and Non-Hodgkin's), Wilms tumour, Rhabdosarcoma and Retinoblastoma. The majority of childhood cancers are not amenable to screening, apart from retinoblastoma (RB) and other rarer heritable conditions. Unlike some adult cancers, childhood cancers are not associated with lifestyle. Emphasis in childhood cancers is early detection as there is high potential for cure. Improved minimum action recommended and attempts made to equip level of care for adequate clinical work up, sampling, specimen referral or and diagnostic work up.

High clinical suspicion required for early comprehensive work-up and review of unresponsive and poor response to treatment leading to referral to county referral and specialist health institutions.

Basic lab investigations such as Total Blood Counts, Peripheral Blood Film, Urea and Electrolytes, Creatinine, Liver Function Tests (enzymes and bilirubin), etc. predate specialist neoplasia diagnostic tests and supplement others as imaging studies.

Specimens and tests in childhood neoplasia suspicion and diagnosis

1. Peripheral blood
2. Peripheral blood film
3. Bone Marrow Aspirate
4. Bone Marrow Biopsy
5. Lymph node Aspirate
6. Lymph node Biopsy
7. Tissue Biopsy... Neck and Jaw masses, etc.
8. Tru-Cut or Kidney Core biopsy
9. Nephrectomy and Partial nephrectomies.
10. Ocular/Globe specimen

Specimen	Who collects	Handling specimen	Reporting	Stains/ preparation
Peripheral blood for counts	Phlebotomist, clinician	EDTA/ purple top tube	Laboratory Technician/ Technologist, Medical Laboratory Scientist.	
Peripheral blood film	Phlebotomist, clinician	EDTA/ purple top tube, clean slides	Hematology Technologist, Pathologist, Hematologist.	Giemsa, Leishman's, MGG, Special stains
Bone Marrow Aspirate	Trained Medical officer or Specialist, Pathologist	EDTA/ purple top tube, clean slides, air dried	Pathologist, Haematopathologist,	Giemsa, Pearle's Prussian Blue, MGG, Special stains
Bone Marrow Biopsy	Trained Medical officer or Specialist, Haematologist, Pathologist	Impression smears and in 10% neutral buffered formalin	Trained Pathologist, Haemato-pathologist	Giemsa, Haematoxylin & Eosin, Pearle's Prussian Blue, MGG, Special stains
Lymph node Aspirate	Trained Medical officer or Specialist, Pathologist	Clean slides, 95% Alcohol/ Propanol	Pathologist, Haemato-pathologist,	MGG, ZN, Special Stains,
Lymph node Biopsy	Trained Medical Officer, Surgeon, Pathologist	Impression smears and in 10% neutral buffered formalin	Pathologist	MGG, Hematoxylin & Eosin, Special Stains including Immunohistochemistry
Tissue Biopsy	Surgeon, Medical Specialist, Oncologist	10% neutral buffered formalin	Pathologist, Specialist Pathologist	Hematoxylin & Eosin, Immunohistochemistry
Tru-Cut Kidney biopsy, Nephrectomy	Surgeon, Urologist, Urology surgeon,	10% neutral buffered formalin Fix nephrectomy specimens overnight	Pathologist	Hematoxylin & Eosin, Special Stains and genetic tests (FISH, Cytogenetics)
Fluids e.g CSF ascitic and pleural Fluids	Clinician	In designated container	Hematoxylin, eosin, Giemsa, ZN, gram stain.etc	Hematoxylin & Eosin, Special stains
Ocular Globe Specimen	Ophthalmologist/Eye specialist	10% neutral buffered formalin	Pathologist/Ocular Pathologist	Hematoxylin & Eosin, Special stains



Specimen Handling, processing and reporting

Lymph node

Useful in primary node, hematopoietic and metastatic disease; treated as small tissue specimen and information including biodata and clinical history is compulsory for accurate reporting. Relevance is per clinical presentation but following important: site, purpose of procedure, size, consistence, gross appearance if resection is done, features of cut sections, prior treatment, investigations and results, immunologic status, cell counts and PBF morphology, etc.

Removal is by Medical officer, Pathologist, primary physician, etc. with minimum pressure (avoidance of crush artefacts) and immediate transverse section perpendicular to the long axis and air-dried impression smears taken on slides for Romansky stains before fixation. Other impression smears taken and alcohol fixed. Specimen to preservative volume about 1:10 in a wide mouth screw cap container. The lymph node should be sectioned. The fresh slides should be submitted for genetic studies while the specimen is fixed in 10% buffered saline for histology, histochemistry, immunohistochemistry stains, etc.

Bone Marrow Aspirate and Biopsy

This is done to evaluate hematologic disease or stage carcinomas and lymphomas. It Provides useful information often in addition to that of lymph node aspirate and biopsy and their reports if present is important. Aspirates handled by trained technologist, laboratory scientist, Medical officer and Pathologist. Smears are prepared immediately and part may be preserved in EDTA tube and pressed within 30min to one hour

The trephine Biopsy is immersed immediately in 10% neutral buffered formalin or other specified preservative. Impression, rolled smears should be made prior to fixation. Pre-embedding processing involves decalcification. Period in fixative and decalcifying fluid critical for sectioning histologic clarity. Stains in addition to H&E depend on clinical information and H&E findings but generally includes PAS, Perl's Prussian blue, reticulin and fungal stains.

Where possible, the sampler in BMA and BM Trephine should report. If not, to package for referral to more equipped center. Clinical notes (thoroughly filled requisition form required) should accompany specimen. Always fresh peripheral blood film and a counter count print out or sample should always accompanies BMA and BM histology specimen. The Specimen should be submitted for flow cytometry.

Tissue biopsy

Tissue biopsies from masses excised from children (e.g. jaw masses, neck swellings, abdominal or other head and neck masses are in principle handled, grossed, trimmed and processed in the same manner as specimens from adults.

Additional stains and immunohistochemistry are usually required for definitive diagnosis of childhood tumors. The particular immunostain will depend on the organ involved, site, and morphology on HE stains.

Trucut Kidney biopsy and Nephrectomy specimens

Trucut biopsies should be counted fixed and processed for histological examination in the usual manner as other biopsies

Nephrectomy specimens should be weighed, described, grossed, and sampled to include the capsule, cortex, cortico-medullary junction, renal pelvis and the renal vein, perirenal fat, and Gerota's fascia. If there is a gross tumor on sectioning, its color, texture, dimensions and location should be described as well as necrosis and gross involvement of the renal vein.

Identify describe and sample the adrenal glands if present.

All hilar tissue should sample for histology.

Ancillary testing in childhood cancer

Ancillary testing in childhood cancer is crucial in arriving at the accurate diagnosis, often because conventional histopathology and hematological procedures are inadequate to pinpoint the definitive cancer. This ancillary testing takes the form of flow cytometry and genetic testing.

The table below shows commonly used ancillary testing techniques for childhood cancer and their sample requirements

Sample requirements for Flow Cytometry and Cytogenetics

NB Most laboratories will have additional information specific to their setup on the sample requirements. It is recommended to contact your referral laboratory prior to sample collection

<u>Test</u>	<u>Sample types</u>	<u>Sample details</u>
Flowcytometry	PERIPHERAL BLOOD, BONE MARROW, CSF, PLEURAL & ASCITIC FLUIDS, FNA, LYMPH NODES, BIOPSY	PERIPHERAL BLOOD: 2 x 5ml heparin (preferable) or 1 x 5ml EDTA (acceptable) BONE MARROW: 2 x 5ml heparin (preferable) or 1 x 5ml EDTA (acceptable) CSF: Plain tube without gel or any other anticoagulant acceptable) CSF: Plain tube without gel or any other anticoagulant MUST REACH FLOW LAB WITHIN 6 HOURS*OF COLLECTION PLEURAL FLUID: Plain tube without gel or any other anticoagulant ASCITIC FLUID: Plain tube without gel or any other anticoagulant FNA: In RPMI transport medium - to keep cells viable LYMPH NODE: In Buffered Saline BIOPSY: In Buffered Saline PLEASE NOTE: Any flow requests must send with copy of REQUEST FORM with as much clinical info as possible
Cytogenetics	Can be performed on BLOOD, CSF,BUCCAL, AMNIOTIIC FLUID, PLEURAL EFFUSION CHORIONIC VILLI, SKIN, NAILS, HAIR FIXED TISSUE SLIDES, (LYMPHNODE,TUMOUR BIOPSY) NB CONTACT LABORATORY FOR SAMPLE SPECIFICS	EXAMPLE:BONE MARROW CYTOGENETICS BONE MARROW ASPIRATE (HEPARIN) AND/OR UNSTAINED SLIDE. Sample must not be older than 2 days. CD 16/19 2xEDTA FISH TEST (Bone Marrow) MYELOMA TRANSLOCATION PROFILE SAMPLE:2 X Edta PCR 1 (9:22) QUANTIFICATION SAMPLE : 2 X EDTA or 2 x PAX gene TUBES PHILADELPHIA CHROMOSOME. SAMPLE: 1 X <u>HEPARIN</u> RED CELL MEMBRANE PROTEIN ANALYSIS SAMPLE: ONE or TWO ACD TUBES - ON ICE (NOT FROZEN) T CELL RECEPTOR GENE RE ARRANGEMENT SAMPLE: 1 x EDTA



CYTO/HISTOPATHOLOGY REPORT FORM

LAB NUMBER

Health facility Name	Sub county	County
Year:	Month	

A PATIENT :

	FIRST NAME	MIDDLE NAME	SURNAME
1. NAME:			

2. Identification No 3. Marital Status 1=Single 2=Married 3=Widowed 4=Separated
5=Cohabiting 6=Divorced 7=Child 9=Unknown

4. TEL NO (Patient) 5. TEL. NO (Nok)

6. Age 7. Date of Birth 8. Sex (1=Male 2=Female 9=Unk)

9. Place of Residence	A. COUNTY	B. SUBCOUNTY	C. VILLAGE/ESTATE

10. Place of Birth 11. Tribe

12. Religion 1=Christian 2=Muslim 3=Hindu 4=Other

13. Education Level

14. Occupation

15. Smoking Status (1=Never 2=Smokes 3=Ex-Smoker 9=Unknown)

16. Drinking Status (1=Never 2=Alcoholic 3=Ex-Alcoholic 9=Unknown)

B TUMOUR

17. Incidence date 18. Basis of Diagnosis 1.- Clinical Only
 2.- Clinic. Invest/radio-image
 4.- Biochem. Immuno test
 5.- Cytology/Haematology
 6.-Histology of metastasis
 7.-Histology of primary
 9.-Unknown

19. Primary Site _____ specimen type _____

20. Laterality 1. Unilat 2. Bil 3.Rt 4.Lt 9.Unk

21. (A) Histology _____

21. (B) CYTOLOGY _____

_____ Morphology code

Pertinent Clinical Information



Ministry of Health SPECIMEN COLLECTION CONSENT FORM

Patients are only expected to consent to the procedure if they understand:

- Why the procedure is needed.
- The type of an aesthetic used (checking for any allergies).
- Wound aspects - patients should be made aware that there is a small chance that the wound might get infected and that this may require further treatment.
- The final cosmetic results cannot be guaranteed as every patient has a completely different healing process as far as final scar appearance is concerned.
- Patients are expected to follow instructions given to care for the wound and avoid the unwanted early openings which will result in unwanted cosmetic result and wound infection.
- Patients are expected to understand they can opt out before the procedure is performed
- Time for removal of the sutures/stitches (if applicable)

Patient Name: _____ Date of Birth: _____ Sex: _____

Address: _____ Phone: _____

PROCEDURE: _____

Complications may include (but are not limited to):

1. Bleeding
2. Infection
3. Delayed healing
4. Scarring
5. Pain

I, _____, consent to the minor surgical procedure as described to me by my Doctor.

I have read and understood the information above and fully understand the reasons for my procedure.

Patients Signature: _____ Date:

D	D	M	M	Y	Y	Y
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Clinician Name (print): _____ signature: _____



M.O.H. NO

MINISTRY OF HEALTH				
Cyto/Histopathology specimen referral form				
Address				
Patient name (Last, First, MI)	Date of birth D D M M Y Y Y	Sex M <input type="checkbox"/> F <input type="checkbox"/>	National identification number	OP/IP number
Patient phone number	Marital status Single <input type="checkbox"/> Married <input type="checkbox"/>	Next of kin name (Last, First, MI)	Next of kin phone number	
County of residence	Smoking status Former <input type="checkbox"/> Current <input type="checkbox"/> Never <input type="checkbox"/>	Drinking status Social <input type="checkbox"/> Overuse <input type="checkbox"/> Never <input type="checkbox"/>	Education Level	Occupation

REFERRING PERSONNEL

Name (Last, First, MI)	Phone number	Email address
SHIPMENT DETAILS	MODE OF TRANSPORT	NAME AND CONTACT OF SHIPPING PERSONNEL
		SIGN
DATE AND TIME OF SHIPMENT	NAME AND CONTACT OF DISPATCHING PERSONNEL	NAME OF SHIPPING INSTITUTION AND STAMP
	SIGN	
SHIPPING TEMPERATURE		
2-80c Room temp.		

RECEIVING REFERENCE LABORATORY

Date and time received	Condition upon reception	
	Suitable	unsuitable
*Reasons for Rejection		
<p>*Where there are inadequate patient, specimen identification and quality the dispatching personnel will be informed and requested to identify the case and provide the necessary details. If the dispatching personnel cannot be contacted, the referral form and specimen will be returned to the sender with a "discrepancy" notice. The dispatching personnel must complete and sign the referral form and must return the corrected form/specimen to the referral facility</p>		

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