COMPARISON RESULTS BETWEEN IMPRINT CYTOLOGY, SCRAPE CYTOLOGY AND BIOPSY IN SURFACE MALIGNANCIES

Dissertation submitted to the

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

In partial fulfilment of the requirements for the degree of

M.S. GENERAL SURGERY – BRANCH I

MAY 2018

CERTIFICATE BY THE GUIDE

This is to certify that this dissertation titled **"COMPARISON RESULTS BETWEEN IMPRINT CYTOLOGY,SCRAPE CYTOLOGY AND BIOPSY IN SURFACE MALIGNANCIES** "is a bonafide research work done by **Dr.M.SENTHILVEL,** in partial fulfilment of the requirement for the degree of **M.S.GENERAL SURGERY – BRANCH I.**

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DECLARATION BY THE CANDIDATE

I solemnly declare that this Dissertation **"COMPARISON RESULTS BETWEEN IMPRINT CYTOLOGY, SCRAPE CYTOLOGY AND BIOPSY"** was done by me in the Department of General Surgery, Thanjavur Medical College, and Hospital, Thanjavur under the Guidance and Supervision of my Professor **Dr.K.SATHYABAMA M.S.**, Department of General Surgery, Thanjavur Medical College, Thanjavur between 2016 and 2017.

This Dissertation is submitted to the Tamilnadu Dr. M.G.R Medical University, Chennai in partial fulfillment of University requirements for the award of M.S Degree (GENERAL SURGERY).

DR. M. SENTHIL VEL

M.S GENERAL SURGERY

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thanks to all the patients who participated in the study. Completion of this work would not have been possible without their co-operations.

CERTIFICATE

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.....&SCRAPE CYTOLOGY WITH BIOPSY IN SURFACE MALIGNANCIES.

submitted by Dr. .....M.SENTHILVEL..... **of**

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was approved by the Ethical Committee.

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ABSTRACT

INTRODUCTION

Origin of cytology dates back more than a century, for over 100 years the discipline of anatomical pathology, has centred on diagnostic histopathology.

Diagnostic cytology is the science of interpretation of cells derived from human body, which either exfoliates freely from epithelial surface or removed from various sources by artificial means.

A correct diagnosis helps in starting the specific therapy in time, thus reducing morbidity and mortality. Imprint and Scrape cytology are now rapid diagnostic tool in the armamentarium of clinician's .Imprint and scrape cytology are simple and rapid techniques for diagnosis.

Imprint is a touch preparation in which tissue is touched on the slide and it leaves behind its imprint in the form of cells on glass slide; studies are made after proper staining.

Scrape cytology is performed by using sterile sticks on the lesion and studies done after slides prepared with staining

This study is undertaken with the aim that though biopsy is Gold standard, imprints and scrape cytology are a rapid, simple and easy technique for tissue diagnosis. This is an accurate diagnostic tool available to all practicing surgeon even in small hospitals and semi urban hospitals

AIMS & OBJECTIVES

To analyze the sensitivity and specificity of imprint and scrape cytology and thereby to evaluate its diagnostic utility in comparison with biopsy results.

MATERIALS AND METHODS

1. SOURCE OF DATA

2. TYPE OF STUDY

3. NUMBER OF GROUPS STUDIED

4. SAMPLE SIZE

5. INCLUSION CRITERIA

6. EXCLUSION CRITERIA

7. PARAMETERS STUDIED

8. PROCEDURE

9. METHOD OF STATISTICAL ANALYSIS

10. ETHICAL CONSIDERATIONS

SOURCE OF DATA

All patients admitted to the Department of General Surgery with clinical evidence of Surface malignancies

These patients were subjected to Imprint/Scrape cytology and biopsy of clinically suspicious Lesions .

Accuracy of Imprint /Scrape cytology results compared with Histopathology.

TYPE OF STUDY

COMPARISON STUDY

NUMBER OF GROUPS STUDIED

Patients admitted with clinically evident surface malignancies in the Department of General Surgery in Government Thanjavur Medical College

SAMPLE SIZE

This study was carried out on 50 patients admitted with Clinically evident surface malignancies for a period of one year from September 2016 to September 2017

INCLUSION CRITERIA

All patients with the following Surface malignancies

Ca Buccal mucosa , Lip, Tongue

Ca Breast with ulceration

Ca Rectum and anal canal

Malignant cutaneous ulcers

Ulcerated neck swelling

EXCLUSION CRITERIA

Patients not willing for study

Patients with Gynaecological malignancies like Ca Vagina and Ca Vulva

PARAMETERS STUDIED

All patients admitted to the Department of General Surgery with clinical evidence of Surface malignancies after relevant history and clinical examination. These patients were subjected to Imprint/Scrape cytology and biopsy of clinically suspicious Lesions after informed consent. Comparison of results by statistical analysis done. Accuracy of Imprint /Scrape cytology results compared with Histopathology.

PROCEDURE

All patients admitted to the Department of General Surgery with clinical evidence of Surface malignancies after relevant history and clinical examination.

These patients were subjected to Imprint/Scrape cytology and biopsy of clinically suspicious Lesions after informed consent.

sterile blade;

sterile gloves

sterile sticks

clear glass slides

glass marking pencil

sterile dressing material

Technique for imprint smear:

The imprints were prepared according to technique described by Tribe.

- Slides properly labelled by glass marking pencil.
- Slides were touched on the surface of the lesion , avoiding a gliding movement. Pressure applied for imprinting varied with the consistency of the specimen.
- Smears were quickly fixed in 95% alcohol in order to avoid air drying artefact and stained with a variant of Papanicolaou's-stain.

Technique for Scrape smear:

- As ulcers are typically covered with a haematic crust containing inflammatory– necrotic cells or debris, the first scrapes must be carried out to remove the superficial debris and after these, other scrapes were gently performed to collect more representative specimens.

- Multiple delicate scrapings were repeated to gradually reach the bottom of the ulcer without excessive bleeding using edge of the glass slide/wooden spatula.
- Smears were quickly fixed in 95% alcohol

Biopsy specimens taken from these patients fixed in 40% formalin. After proper fixation samples were processed by routine histopathological processing and sections were stained by Hematoxylin and Eosin

THE PROFORMA FOR STUDY:

Name:

Age/Sex:

Clinical diagnosis:

Imprint cytology:

Scrape cytology:

Biopsy report:

Comparison of results by statistical analysis done:

Accuracy of Imprint /Scrape cytology results compared with Histopathology:

METHOD OF STATISTICAL ANALYSIS:

- AGE DISTRIBUTION
- CASE DISTRIBUTION
- SENSITIVITY
- SPECIFICITY
- POSITIVE PREDICTIVE VALUE
- NEGATIVE PREDICTIVE VALUE

ETHICAL CONSIDERATIONS:

- Consent obtained from the patients after assuring the non harmfulness and confidentiality of the study
- Patients are assured that the details of the study were only used for academic purpose

REVIEW OF LITERATURE

Rapid and accurate diagnosis is of paramount importance in the outcome of medical care. Though the histopathology remains the gold standard , the imprint /scrape cytology is one of the rapid methods that can be used in the diagnosis of benign and malignant lesions in shorter period. A correct diagnosis helps in initiating the specific therapy in time, thus reducing morbidity and mortality. Histopathology is the gold standard means of establishing a definitive pathological diagnosis, whereas use of cytology is controversial. In present study we have correlated the cytological diagnosis by imprint/scrape cytology with histological diagnosis and tried to evaluate the accuracy and usefulness of this method.

For centuries, tissue diagnosis was restricted to macroscopic examination of autopsy material and a limited range of surgical specimens. Microscopic examination of human tissue from autopsies and surgical procedures was introduced in the nineteenth century. Analysis of tissue samples is now an integral part of clinical management. Tissue diagnosis is usually the responsibility of a histopathologist (or 'pathologist'), who is a medically qualified practitioner. The specialty now known as histopathology (or sometimes cellular pathology) encompasses histopathology, cytopathology and autopsy work and is heavily dependent on microscopy.

In the UK, the nature of the histopathologist's work has changed since the

1960s. There has been a steady increase in biopsy numbers, partly because of flexible endoscopy. Many resection specimens are assessed with management and prognosis in mind, the diagnosis having been made preoperatively. Screening programmes have had a major impact. New techniques have improved the quality and value of histopathological assessment, while autopsies have steadily decreased in number. Published minimum standards for the assessment of a specimen,e.g. a cancer resection, are often in place. In addition, histopathologists are increasingly involved in multidisciplinary patient management meetings.

A modern histopathology department is usually located in a medium-sized or large hospital. Typically, more than 80 per cent of specimens are from the gastrointestinal tract, gynaecological tract or skin. In line with clinical services, highly specialised work, e.g. neuropathology, is confined to major regional centres.

REASONS FOR ASSESSMENT OF TISSUE

A new diagnosis may be made, e.g. squamous cell carcinoma, or a known diagnosis confirmed. Microscopic clues may be found, e.g. granulomatous inflammation. Additional expected or unexpected diagnoses may be made. For example, biopsies from a patient with inflammatory bowel disease are taken to confirm the diagnosis and exclude dysplasia but might reveal additional

findings, e.g. cytomegalovirus. An appendix removed for appendicitis could contain an incidental carcinoid tumour. Tissue analysis also helps to determine treatment and prognosis. For example, a liver biopsy from a patient with chronic viral hepatitis is not taken to make the diagnosis but instead helps to determine therapy, exclude other diseases (e.g. steatohepatitis) and exclude complications of chronic liver disease (e.g. neoplasia).

The pathologist's assessment of resections also helps surgeons to audit their performance. A tissue sample does not necessarily represent the entire patient. The interpretation of microscopic changes may be considerably enhanced by correlation with the macroscopic findings and the clinical picture. Accordingly, a request form with adequate clinical details should accompany all specimens. Essential details include site of biopsy, date of birth, gender, medications, relevant risk factors and past medical history.

Summary box 15.2

Common types of tissue sample

- Histology
  - Formalin-fixed tissue
    - Biopsy
      - Mucosal
      - Punch
      - Needle (core)
      - Currettings
      - Excision
    - Resection
      - Small
      - Large
  - Fresh tissue (usually for frozen section)
- Cytology
  - Cervical
  - Washings, brushings, scrapes
  - Fine-needle aspirate (FNA)
  - Fluids/sputum

HISTOLOGY

Specimens for histology are arbitrarily classified as biopsies and resections, although the word ‘biopsy’ can refer to any tissue sample. Types of biopsy include punch biopsy, needle core biopsy and mucosal biopsy. An excision biopsy serves as both a diagnostic biopsy and a small resection. Samples for routine histology are immediately placed in a fixative, usually formalin (10 per cent formaldehyde), to preserve morphology.

CYTOLOGY

Cytological specimens can be obtained from many sites using a variety of approaches. Some are easy to obtain, e.g. urine and sputum, whereas others require more intervention. A conventional cervical smear is obtained by sampling the cervical transformation zone with a brush/broom. Bronchial aspirates, washings and brushings, and gastrointestinal and biliary brushings sample a relatively wide area and may therefore be useful for the diagnosis of neoplasia. Fine-needle aspiration (FNA) cytology may sample accessible sites such as the breast, thyroid and superficial lymph nodes, while FNA from deeper and less accessible structures, e.g. liver, pancreas, kidney and lung, is usually assisted by ultrasound or computed tomography (CT) guidance. Ultrasound-guided transbronchial FNA may be used for mediastinal masses and transmucosal FNA for submucosal gastrointestinal lesions or perivisceral lesions. Fluids may be submitted directly to the laboratory for cytological assessment.

FRESH TISSUE

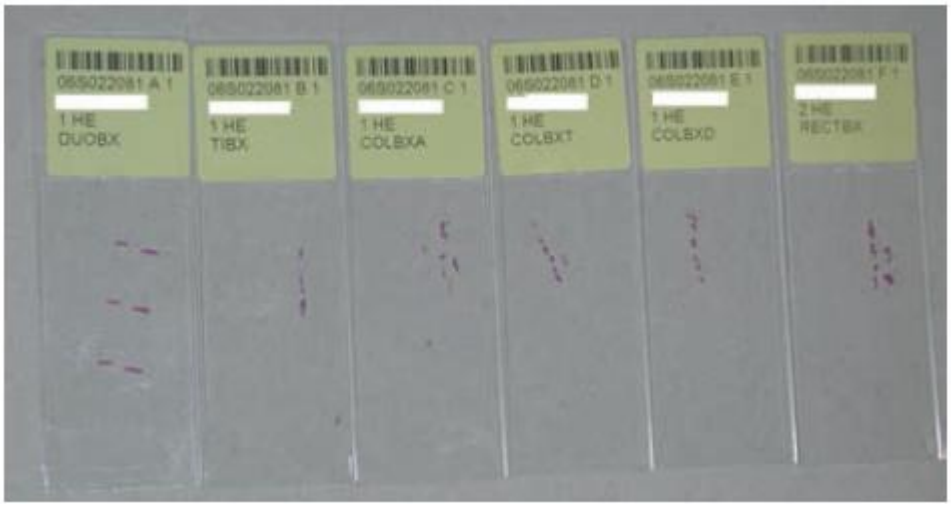
The most common indication for submission of a fresh tissue sample (i.e. without fixative) is rapid frozen section diagnosis, but other indications are microbiological assessment, electron microscopy, chemical analyses (e.g.

quantification of iron) and various types of molecular pathological analysis. Before fixing a histology or cytology specimen, the operator should ask whether any of these investigations might be useful.

RISK MANAGEMENT

Safety and risk management are priorities in the laboratory. Any risk of contamination by transmissible infection, e.g. hepatitis B virus, HIV, must be minimised by the use of warning labels, especially when fresh tissue is being submitted. Formalin kills many micro-organisms, but any risk of infection should still be notified. Also, formalin itself is toxic to the eyes and skin.

Accordingly, leaking or faulty specimen containers should be discarded. Containers must be labelled with the patient's details to avoid errors of identity



SPECIMEN PROCESSING

Histology specimen

On arrival in the histopathology department, specimens are given a unique number and submitted for macroscopic assessment and sampling (‘cut up’). The largest specimens are opened (e.g. bowel) or sliced (e.g. uterus) and left to fix in formalin for at least 1 day. Once fixed and in a suitable condition for cutting, a text description of the specimen and any visible lesion is made. Representative samples (‘blocks’) are taken from any specimen too large to be processed whole. This is usually done by a histopathologist, especially if a case is complex, but sometimes by non-medical staff. A local or national protocol for sampling is often followed. For example, samples from most types of cancer include resection margins, tumour, lymph nodes, non-neoplastic tissue, and any other abnormal areas. Coloured inks may be used to identify resection margins and surfaces.

Specimens, or samples from specimens, are placed in plastic cassettes and then embedded in paraffin wax while in the cassette to make a tissue block. Sections with a thickness of approximately 5 μm (microns) are cut from the block using a microtome. The sections are placed on a glass slide and stained with haematoxylin and eosin (H&E). This work is done by trained staff, known in the UK as biomedical scientists (BMSs). High standards are necessary because a poorly cut section may have various artefacts, such as lines

and folds, which impede accurate assessment. H&E as the first line stain has stood the test of time, probably because it is inexpensive, safe, fast, reliable, familiar and informative.

The stained sections are examined with a microscope by a histopathologist, who correlates the histological features with the clinical details and with the macroscopic description.

Histological processing: sequence of events

- Biopsy or resection specimen received
- Description made
- Specimen sampled (unless small enough to submit in its entirety)
- Specimen or samples placed in cassette(s)
- Paraffin wax block(s) made
- 5-μm sections cut
- Sections put on glass slides
- Sections stained with H&E
- Histopathologist examines slides
- Histology compared with clinical and macroscopic findings
- Further studies if necessary
- Report entered onto computer system
- Report authorised or signed

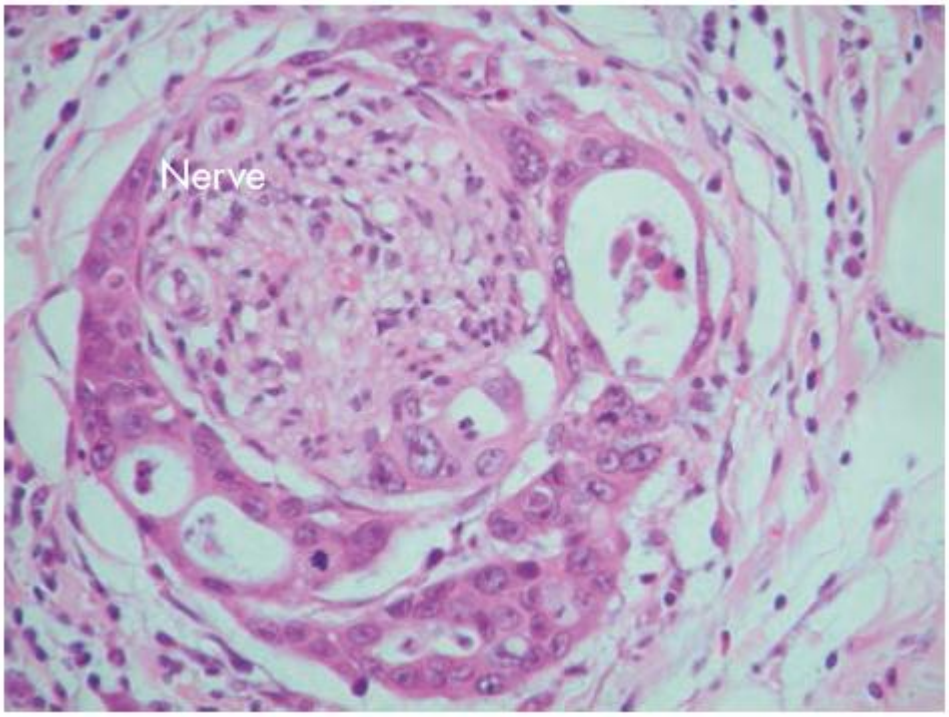
Cytology specimen

Many samples for cytology can be smeared immediately onto glass slides, fixed (usually in alcohol) or air dried, and stained immediately or later. Several slides are usually produced, some of which are stained with a Papanicolaou (Pap) stain

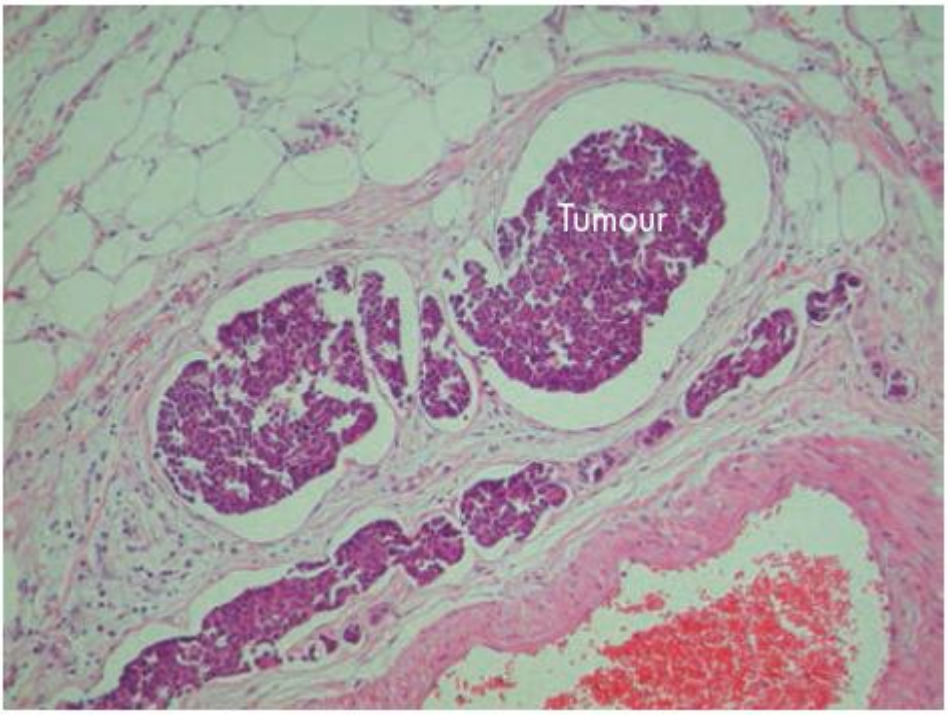
and some with another method such as May–Grünwald–Giemsa (MGG) or Romanowsky. Pap stain is regarded as the preferred stain for fixed specimens while MGG is better for air-dried material. Often the sample will be stained with both. Cervical smears are usually stained with a Pap stain only. There has been a move towards liquid-based thin-layer technology for many samples. For liquid-based cytology, the sampling device is usually washed in a liquid medium and the material obtained is then processed in the laboratory.

Microscopic features of malignancy

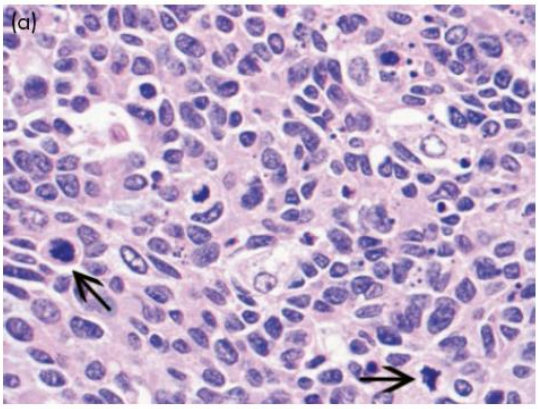
- Metastasis
- Invasion
  - Of surrounding tissue
  - Vascular
  - Perineural
- Architectural abnormalities
- Necrosis
- Numerous mitotic figures
- Atypical mitotic figures
- Nuclear abnormalities
  - Pleomorphism
  - Enlargement
  - Hyperchromaticity
  - Chromatin clumping
- Nucleolar enlargement and multiplicity

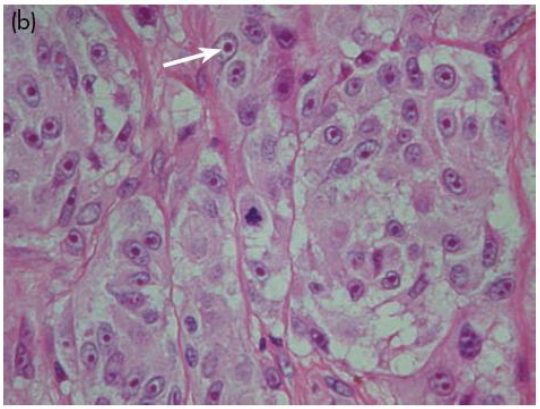


PERINEURAL INVASION



VASCULAR INVASION





NUCLEAR PLEOMORPHISM

CAUSES OF FALSE-POSITIVE DIAGNOSES OF MALIGNANCY

- Interchanged samples
- Contamination
- Interpretative error
- Treatment-induced change

ASSESSMENT

Light microscopy

Most tissue assessment depends on conventional light microscopy. Microscopes have several lenses with various powers of magnification, typically ranging from ×20 to ×400 or more. A low-power lens allows a sample to be scanned and its overall architecture to be assessed, while a high-power lens allows a closer and more detailed view. A teaching arm and a camera can be attached to most microscopes. Polarisation can be used to detect foreign material (e.g. sutures) or to assess a special stain (e.g. Congo red).

Histological assessment

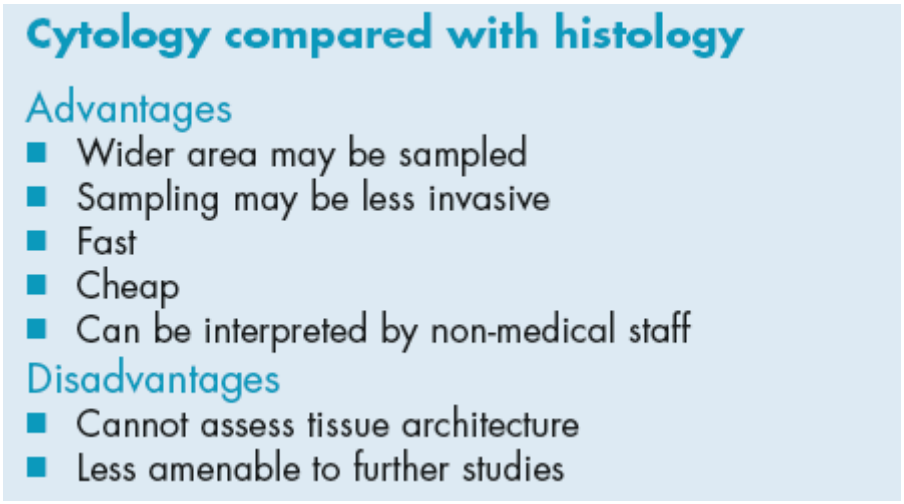
In a histological preparation, the microscopic structure of the tissue is preserved, allowing direct visualisation of architecture. Accordingly, the pathologist can see not only the characteristics of the cells that form the tissue, but also the way in which these cells are related to one another and the way in which different tissue compartments are arranged.

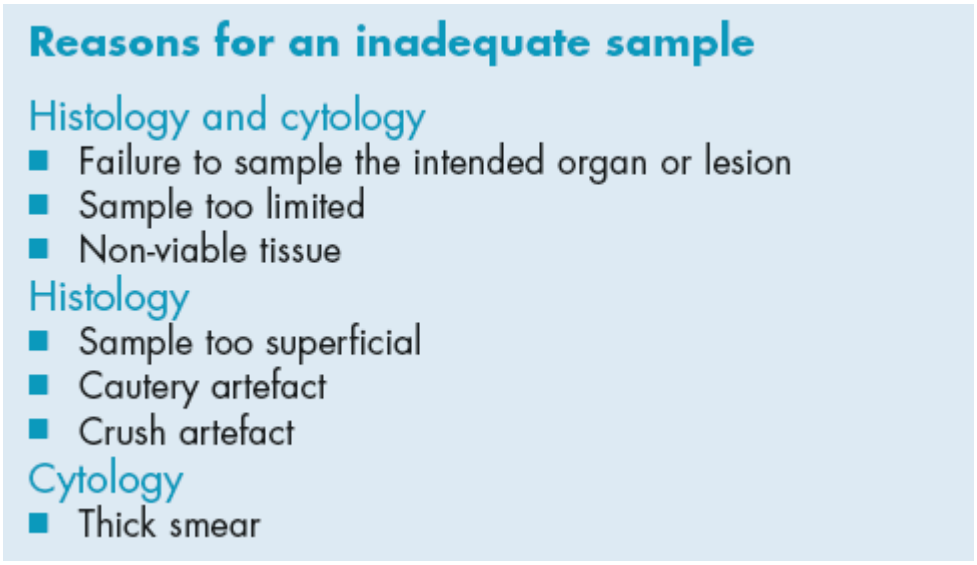
Cytological assessment

A cytological preparation consists of a sample of cells. Architecture cannot be determined, because intact tissue is absent or sparse. Therefore, assessment relies mainly on the characteristics of the cells themselves. Accordingly, it may be difficult to diagnose malignancy because many of the criteria, particularly invasiveness, cannot be assessed. However, cytology has several potential advantages over histology. A wider area may be sampled, and obtaining a specimen may be easier and less traumatic. Processing times are usually shorter and costs lower.

Screening

Screening programmes aim to detect and treat pre-malignant tissue changes, e.g. dysplasia, or early stage malignancy (rather than advanced disease). They may rely on cytology, histology or both. The largest is the cervical cancer programme, which uses cytology initially, with biopsy and histology follow up if appropriate. The breast cancer screening programmes may use cytology and/or histology, while the bowel cancer screening programmes and screening for cancer in ulcerative colitis rely on histology.





SPECIAL STAINS

A ‘special stain’ is a stain that is not routine. Immunohistochemical stains are conventionally excluded from this category. Some special stains demonstrate normal substances in increased quantities or in abnormal locations. The periodic acid–Schiff (PAS) stain demonstrates both glycogen and mucin, whereas a

diastase periodic acid–Schiff (D-PAS) stain demonstrates mucin, e.g. in an adenocarcinoma. Perls Prussian blue stain demonstrates iron accumulation , e.g. in haemochromatosis. A reticulin stain helps to demonstrate fibrosis. Elastic stains also show fibrosis and can highlight blood vessels by outlining their elastic laminae. Special stains can also reveal the accumulation of abnormal substances, e.g. a Congo red stain for amyloid.

IMMUNOHISTOCHEMISTRY

Immunohistochemistry, which was introduced in the 1970s, has had a major impact on histopathological diagnosis. This technique detects a specific antigen using an antibody. The antibody is labelled with a dye and when bound to its target antigen is seen in the tissue section as a coloured stain, often brown. This allows the presence, tissue distribution and cellular localisation of an antigen to be determined. Immunohistochemistry can be applied to fixed and frozen tissue and to cytological preparations. It is specific, safe, quick and relatively inexpensive. However, false-positive results can result from non-specific staining or from crossreaction with similar antigens.

Some immunohistochemical stains used for tumours

- Cell type/site of origin:
  - Epithelial (carcinoma): cytokeratins
  - Lymphoid (lymphoma): CD45, CD3, CD20
  - Melanocytic (melanoma): S100
  - Neuroendocrine: synaptophysin, chromogranin
  - Vascular: CD31
  - Myoid: desmin, actin
- Site of origin/cell type:
  - Prostate: prostate-specific antigen (PSA)
  - Lung: thyroid transcription factor-1 (TTF-1)
  - Thyroid: thyroglobulin
  - Colorectum: cytokeratin 20 (CK20), CDX2
  - Liver: HepPar
  - Gastrointestinal stromal tumour (GIST): CD117, DOG-1
- Prognosis and treatment:
  - Breast carcinoma: receptors (ER, PR, HER2)
  - Endocrine tumours: Ki67 proliferative index

	SCRAPE/IMPRINT	**TISSUE BIOPSY**
MATERIAL	Cells	Tissue
COST	Minimal	Expensive
ANAESTHESIA	Not necessary	May be necessary
EQUIPMENT	Minimal	Extensive
SAMPLING ERROR	Possible	Rare
COMPLICATIONS	Rare	Uncommon
HOSPITAL ADMISSION	Outpatient procedure	May need admission in the hospital
ANCILLARY STUDIES	Possible	Possible

ELECTRON MICROSCOPY

Electron microscopy allows tissue to be visualised at very high magnification, e.g. ×1000 to ×500 000. It may help to decide the lineage of a non-neoplastic or neoplastic cell in difficult cases, and may help to determine the nature of abnormal deposits, e.g. in renal disease. Unfortunately, it is time-consuming,

labour intensive and expensive, and is now used very selectively.

IN SITU HYBRIDISATION

In situ hybridisation (ISH) uses a labelled oligonucleotide probe targeted at a specific RNA or DNA sequence. It can be performed on fixed or fresh tissue sections, allowing the presence or absence of a particular sequence and its location to be determined. Viral genomes, e.g. EBV, CMV and human papillomavirus, can be detected using this approach.

INTERPHASE CYTOGENETICS

This technique is relatively safe and fast and has largely replaced conventional cytogenetics for the analysis of chromosomal changes. It relies mainly on fluorescent *in situ* hybridisation (FISH) (named after the probe's fluorescent label), but also silver *in situ* hybridisation (SISH) and other methods. Fresh and fixed histological material and cytological preparations can be used, the latter typically yielding better results. The probe can target centromeres in order to assess numerical or structural chromosomal abnormalities or can target specific genes.

The technique is used (alongside immunohistochemistry) to detect HER2 amplification in breast cancer and, more recently, in advanced gastric cancer. The results inform the selection of therapy. Other uses include detection of chromosomal gains, losses, and translocations in tumours (e.g. haematological

malignancies) and non-neoplastic conditions (e.g. trisomy 23) and loss of specific gene regions in tumours (e.g. 1p and 19q in oligodendrogliomas).

POLYMERASE CHAIN REACTION-BASED AND RELATED TECHNIQUES :

The PCR amplifies DNA, yielding millions of copies from a single copy of a selected target. The amplified DNA is detected using various techniques, e.g. electrophoresis. RNA can also be amplified, using the technique of reverse transcriptase polymerase chain reaction (RT-PCR). PCR is highly sensitive, fast and safe. However, it is expensive and has a high chance of contamination with DNA from outside sources. PCR can be performed on non-tissue samples (e.g. peripheral blood) and on homogenised fresh tissue. DNA or RNA extracted from formalin fixed tissue may be of lower quality but is also widely used. PCR has many clinical applications, particularly the detection of gene mutations and amplifications and the confirmation of clonality in tumours.

IMPRINT CYTOLOGY

The technique of imprint cytology has provided great impetus to cytodiagnosis due to its simplicity, cost effectiveness, rapid results.

Points to improve the accuracy :

The tissue surface to be imprinted should be flat and there should be no portion of fat protruding from the edges as these tend to smudge the imprint.

2. Sometimes the first imprint contains excess tissue fluid and blood and it was found that subsequent imprints give better cytological results.

3. The ease with which any tumor gets imprinted varies considerably. In order to obtain imprint smears of one cell thickness, the amount of pressure applied at the time of imprinting varies. Benign looking lesions usually require more pressure in order to obtain sufficient cells for diagnosis while malignant tumors get imprinted more easily.

4. Malignant tissue imprints were more cellular than those of benign looking lesions.

Advantages

(1) The procedure for imprint cytology can be done even with poor infrastructure.

(2) Analysis of an individual cell is performed by imprint cytology. It provides an immediate result with minimal artifacts, It is cheaper and so it is most commonly used.

(3) A precise diagnosis is received through this technique.

Disadvantages

The depth of infiltration cannot be analyzed with imprint cytology.

Tumors and well-differentiated tumors with dense fibrous stroma cannot be interpreted through this method.

SURFACE MALIGNANCIES STUDIED

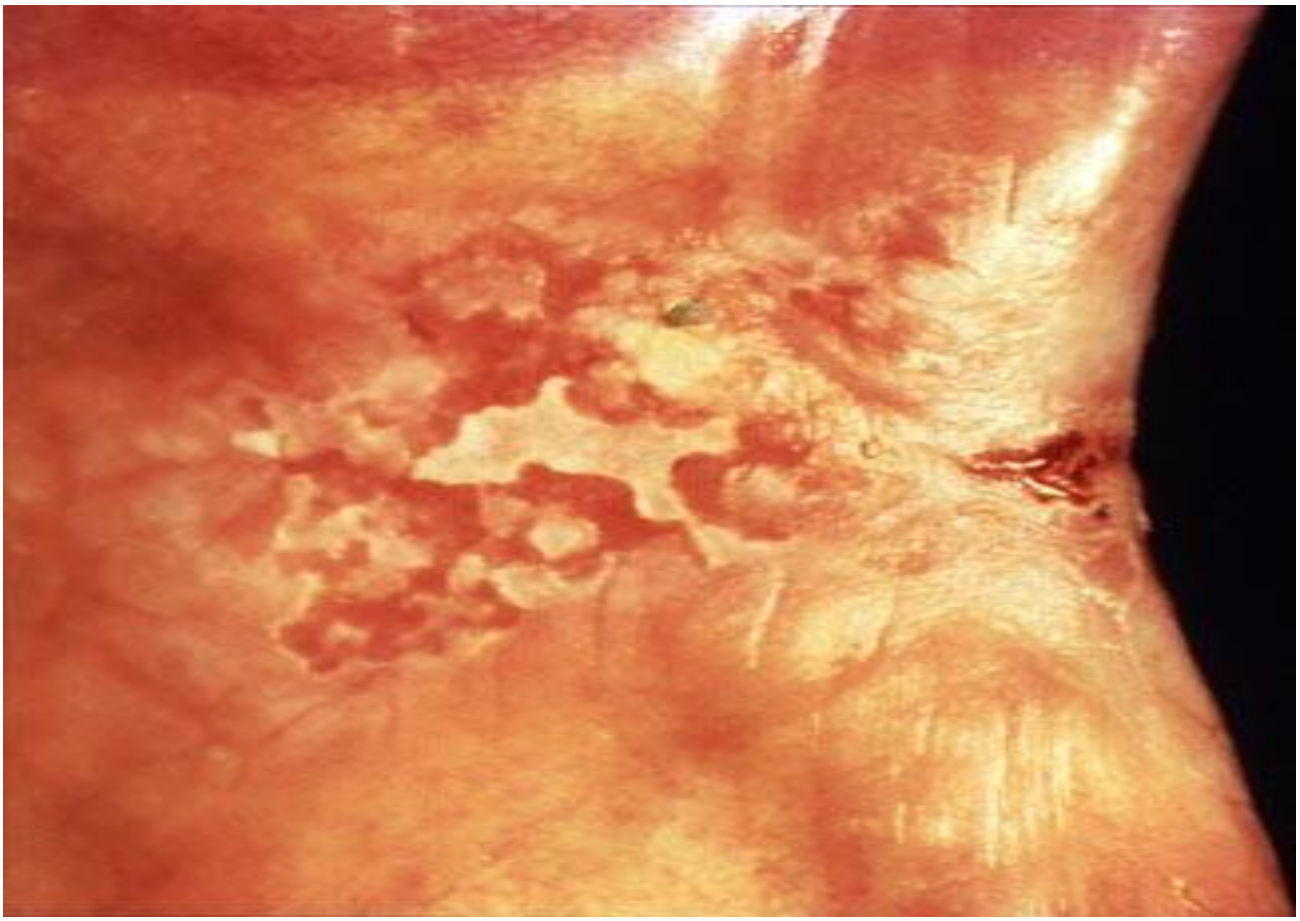
ORAL MALIGNANCIES

- The Oral cavity extends from vermillion border of lips to plane between junction of hard palate and soft palate which includes :Buccal mucosa, upper and lower alveolar ridges ,oral tongue, gingiva, retromolar trigone, floor of mouth, hard palate
- Oral malignancies account for 40% of Head and Neck cancer and ranked eighth among the most common malignancies in the world. The age of onset is around 6^{th} -7^{th} decade . High incidence is seen in India, SE Asia.
- In India ,20 Per 100000 population are affected by oral cancer which accounts for about 30% of all types of malignancies. Around 5 people in india die everyday due to oral malignancy.

PREMALIGNANT LESIONS :

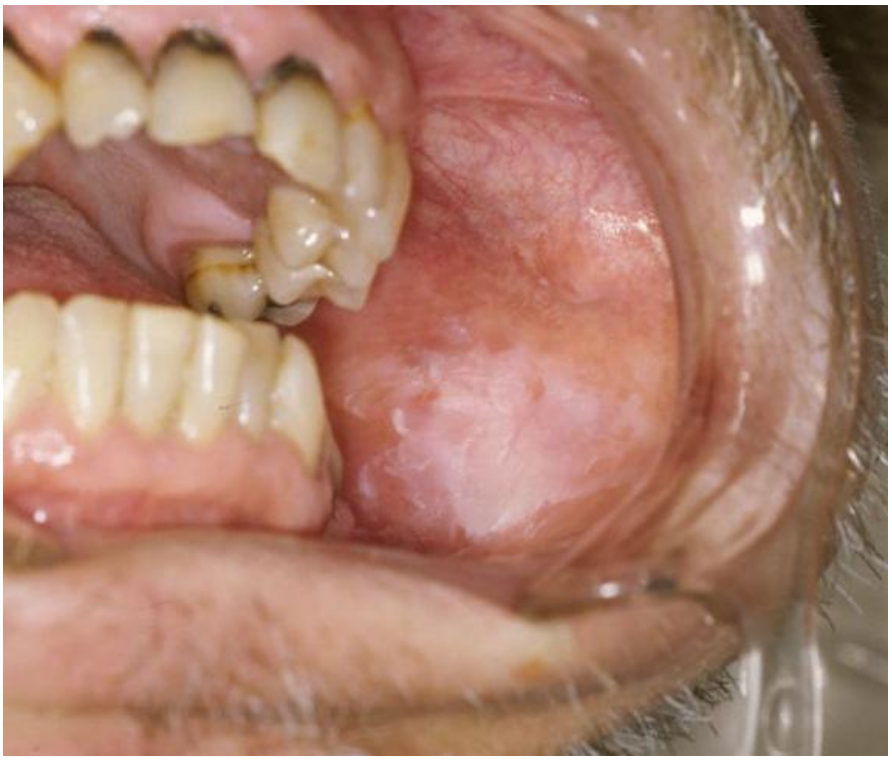
Erythroplakia - non-inflammatory erythematous plaque

Lip, tongue, or floor of the mouth lesions are prone for progression to SCC



- **Leukoplakia -** chronic, white, verrucous plaque with histologic atypia

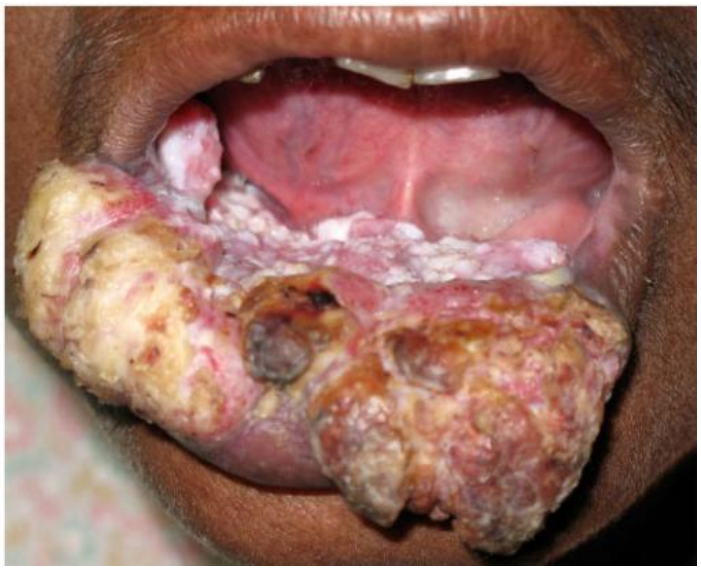
5 - 10 % progress to SCC



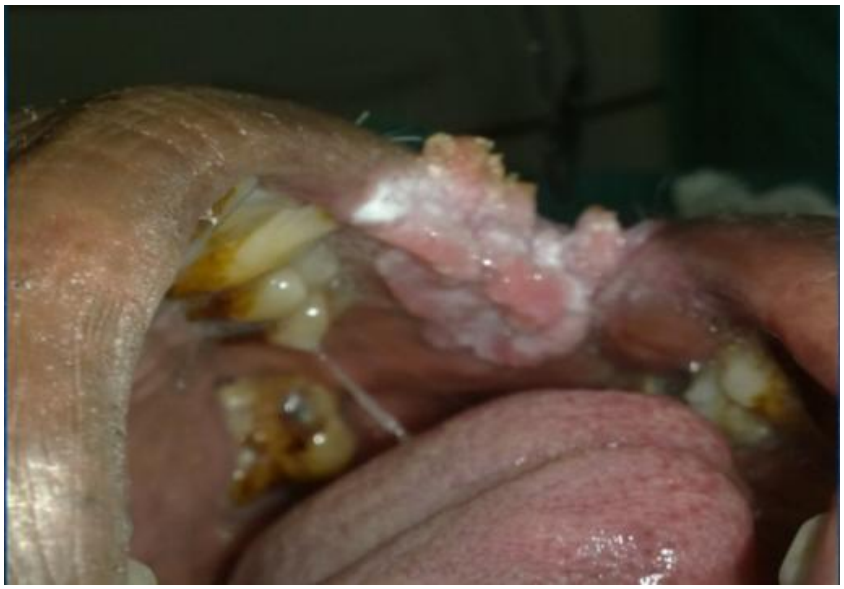
- **Submucous fibrosis**-generalized white discoloration of oral mucosa with progressive fibrosis leading to painful mucosal atrophy and restrictive fibrotic bands which ultimately results in trismus, dysphagia and severe xerostomia

CANCEROUS LESION OF ORAL CAVITY:

SCC 90%



Lips –SCC, Melanoma, BCC(rare) <5% low grade, slow growing rarely



metastasizes with tendency to invade deep tissue.

ETIOLOGY

About 90% of people with oral cavity and oropharyngeal cancer use tobacco and tobacco products. Drinking alcohol strongly increases a smoker's risk of developing oral cavity and oropharyngeal cancer. More than 30% of patients with cancers of the lip have outdoor occupations associated with prolonged exposure to sunlight. Long-term irritation to the lining of the mouth caused by poorly fitting dentures and sharp teeth

Risk Factors

- **Poor nutrition**: A diet low in fruits and vegetables is associated with an increased risk
- **Age**: The likelihood of developing oral and oropharyngeal cancer increases with age, especially after age 35
- **Gender**: Oral and oropharyngeal cancer is twice as common in men as in women
- **Immunocompromised people**
- **Human papillomavirus (HPV) infection:** Commonly affects younger age groups , male, non smokers. High risk HPV-16 predominate type. Association strongest for Oropharynx, specially cancer of tonsils followed by base of tongue.

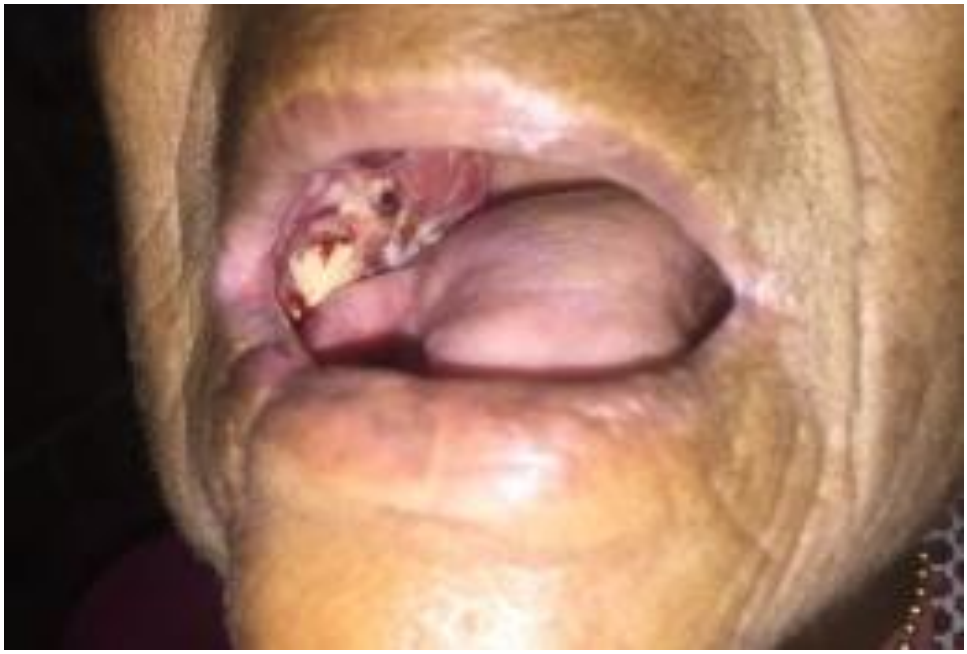
INHERITED RISK FACTORS are

Tumor suppressor gene(p53) defect: Li Fraumeni syndrome.

Defective DNA repair mechanism: Xerodermapigmentosa, ataxia telangiectasia, bloom syndrome, fanconi syndrome. ABO blood groups :Blood group A had 1.46 times higher risk of developing oral cancer as compared with other blood group.

COMMON SITES are

Lips: lower-93%, upper-5%, commissure- 2%



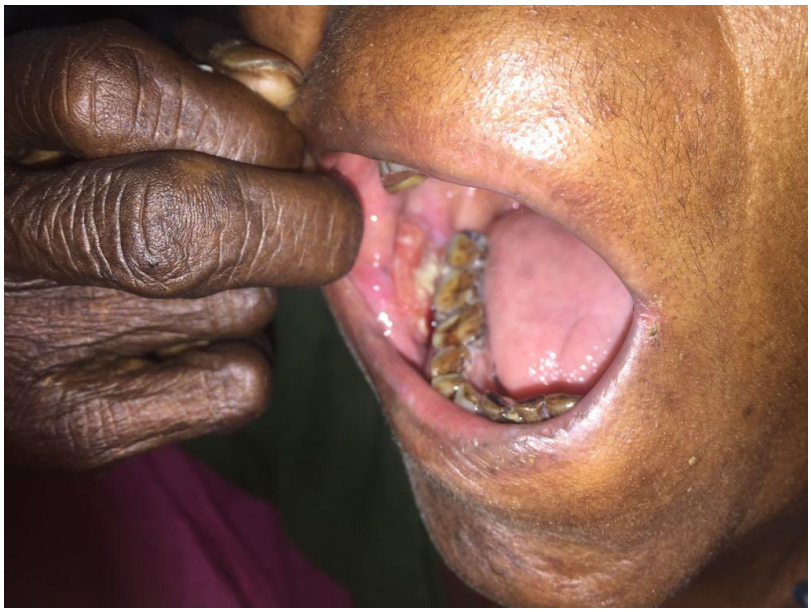
RMT: 2%

Upper alveolus/hard palate: 8%

Buccal mucosa: 10%

Lower alveolus: 15%

Floor of mouth: 30%



Tongue : 35%

Patient need the following Investigations: for staging- CT neck ± CT chest- MRI- USG of neck or primary ± USG guided FNAC of suspicious lymphadenopathy

STAGING OF THE DISEASE :

TNM STAGING -

Primary tumour (T)

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma *in situ*
T1	Tumour <2 cm in greatest dimension
T2	Tumour >2 but <4 cm
T3	Tumour >4 cm but <6 cm
T4	Tumour invades adjacent structures, e.g. mandible, skin

Regional lymph nodes (N)

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node <3 cm in greatest dimension
N2a	Metastasis in a single ipsilateral lymph node >3 cm but not more than 6 cm
N2b	Metastasis in multiple ipsilateral lymph nodes, none >6 cm in greatest dimension
N2c	Metastasis in bilateral or contralateral lymph nodes, none >6 cm in greatest dimension
N3	Metastasis in any lymph node >6 cm

Distant metastasis

M0	No evidence of distant metastasis
M1	Evidence of distant metastasis

Stage			
0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
III	T3	N0	M0
	T1, T2, T3	N1	M0
IV	T4	N0	M0
	Any T	N2	M0
	Any T	N3	M0
	Any T	Any N	M1

Treatment goals:

To eradicate primary tumor and LN metastasis,

Reconstruction to maintain form and function

TUMOR FACTORS AFFECTING TREATMENT

The prognosis depends on the site, size(T stage), location, multiplicity, histology, grade, depth of invasion, pathological features, Status of cervical lymph nodes Proximity to bone

TREATMENT

The Mainstay of treatment for oral malignancies is surgical management:

Wide local excision+/- Chemoradiotherapy

Surgical approach depends on the tumor size, tumor site ,proximity to mandible or maxilla ,Need for neck dissection ,Need for reconstructive surgery.

Chemotherapy drugs commonly used are cisplatin, carboplatin, 5flurouracil,paclitaxel,docetaxel.

Immunotherapy commonly given include IL 2/IRX 2,BCG vaccine

Targeted therapy

Anti-EGFR MoAbs : cetuximab , pantimumab, zalutumumab

EGFR targeted tyrosine kinase inhibitors: gefitinib, erlotinib

EGFR & HER-2 combined tyrosine kinase inhibitors: lapatinib, BIBW-2992. -

VEGFR inhibitor: bevacicumab, sorafenib, sunitinib

MALIGNANT SKIN TUMOURS

Malignant skin tumors most commonly arises from the epidermis

- TYPES

Basal cell carcinoma

Squamous cell carcinoma

Malignant melanoma

Skin adnexal tumors are rare

Chemical carcinogens play a major role

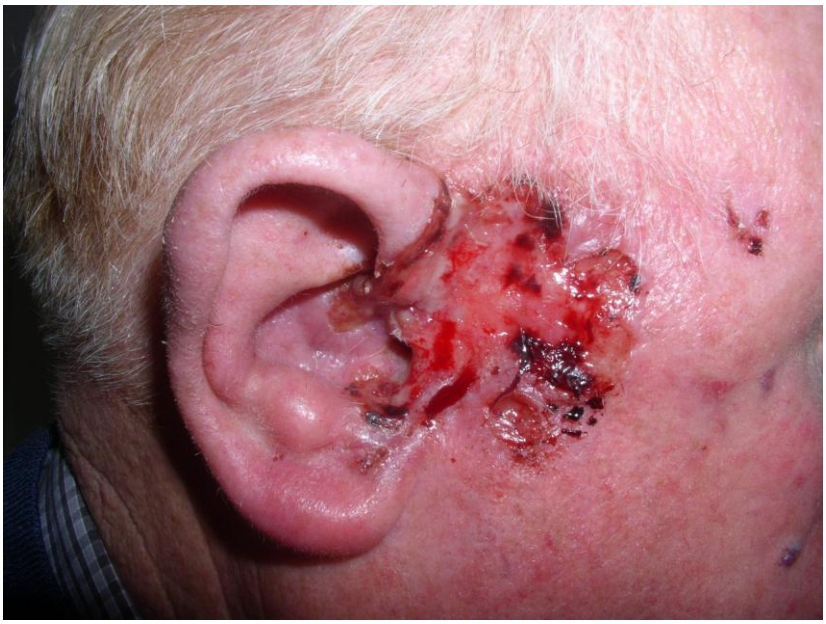
Basal cell carcinoma (RODENT ULCER)

Basal cell carcinoma (BCC) is a malignant tumour of the skin arising from basal cells in the epidermis. BCCs are very common slow growing tumours,locally invasive particularly in those exposed to ultraviolet light. They usually appear after the age of 50 90% are found on the forehead, face and hair margin.

Clinical findings:

BCCs present as small nodules that soonbecome ulcerated centrally, producing an umbilicated lesion.A history of a lesion that apparentlyheals only to recur soon. As the lesion progresses large areas of ulceration with slightly raised pearly coloured edges develop. Untreated, large areas of the face may be eaten away with invasion of bone and Cartilage. ***BCCs do not ,however, metastasize***.

The diagnosis is made clinically but if there is any doubtbiopsy may be obtained prior to definite treatment.



TYPES

- Nodulocystic - Waxy , cream coloured with rolled, pearly borders surrounding central ulcer
- Morpheaform -Type IV collagenase and spread rapidly.Flat, plaque like lesion
- Basosquamous variant - Highly aggressive. Metastasize similar to SCC and aggressive treatment required

If the size of the lesion is more than 2cm,the risk of Basal cell carcinoma is more. Specific location are nose ,ear, eyes. margins are usually Ill-defined and they are more prone for recurrence.

Management of BCC

- Surgery is the mainstay of treatment which involves Complete tumor removal , with pathological confirmation and margin analysis. Large tumors invading adjacent structure with aggressive histology needs WIDE LOCAL EXCISION with 1cm margin.
- MOHS Micrographic Surgery Excision of skin cancer under microscopic control. Minimise recurrent rates with maximum conservation.

Poorly demarcated lesions, lesions located Near vital structures , Recurrent / incompletely excised, Can also be used for squamous cell carcinoma, lentigomaligna.

Non Surgical management consists of laser vapourisation, electrodessication, Curettage

Other Modalities: Topical treatments,Cryotherapy,Imiquimod,5-fluorouracil and Radiotherapy also plays an important role.

Squamous cell carcinoma

Squamous cell carcinoma (SCC) of the skin arises fromthe keratinocytes in the epidermis. It grows rapidly with anaplasia, local invasion and metastases.

Solar keratoses and Bowen's disease are precursors of SCC of the skin .

SCC also occurs mostly on the exposed areas ofthe body (75% on the head, 15% on the hands)

These are aggressive tumours thatwill invade the structures deep to the dermis with metastasesto regional lymph nodes .

Establishing the diagnosis is the first step in the management

of SCC. This is done by obtaining a biopsy forhistological diagnosis

Microscopic Appearance

KERATIN PEARLS - Irregular masses of squamous epithelium proliferate and invade dermis . Perineural / vascular invasion. Positive for cytokeratin 1 and 10Border's histological grading-Ratio of pleomorphic and anaplastic to normal cells

Prognosis

Perineural and vascular involvement. Invasion - Surface size> 2cm

Depth – deeper lesion , worse the prognosis

Lips and ears – increase recurrent rate Histological grade> Immunosuppression

TNM Classification

Size

• T1 - <2cm • T2 - 2-5 cm • T3 - >5cm • T4 - muscle or bone involvement

Nodes

• N0 - no regional nodes • N1 - regional nodes

Metastasis • M0 - no metastasis • M1- distant metastasis

Grade • G1- low grade • G2moderately differentiated • G3- high grade

Surgical excision -Accurate histology.Margins to be assessed

< 1 cm clearance for lesions >2cm.<4cm lesion – 2cm clearance

Veruccus carcinoma - Radiotherapy resistant

Malignant melanoma

Malignant melanoma is a malignant tumour arising from

the melanocytes wherever melanocytes exist leptomeninges Retina Bowel mucosa, melanoma can occur. Approximately 50% of all melanomas

arise in pre-existing naevi and exposure to intense ultraviolet

radiation from sunlight is the most important

aetiological factor. Fair-skinned people

are affected most often.

Types Of Malignant Melanoma

1.Superficial spreading

2.Nodular melanoma

3.Lentigomaligna melanoma

4.Acrallentiginous melanoma

5.Amelanotic melanoma

6.Desmoplastic melanoma

Superficial Spreading Melanoma

Commonest type – 70%

Arise from pre – existing nevus

Rapid growth of darker pigmented are in a junctional nevus.

Predominantly radial growth phase.

Nodularity can occur in vertical growth phase.

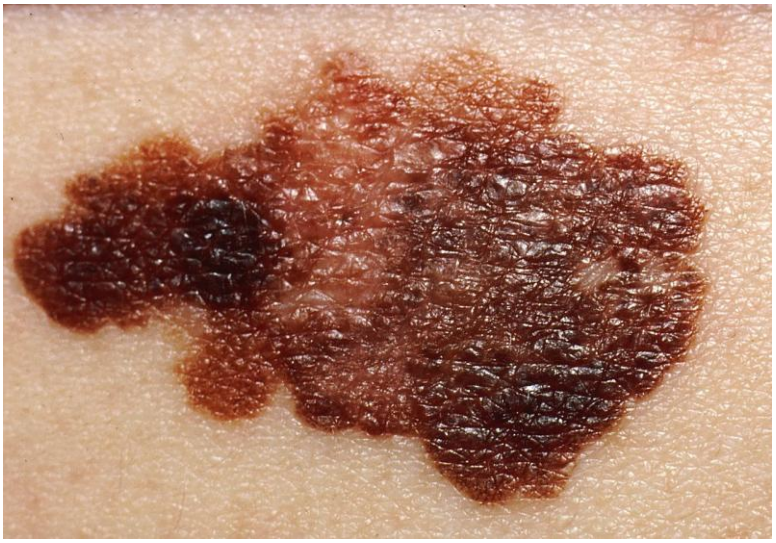
Nodular Melanoma

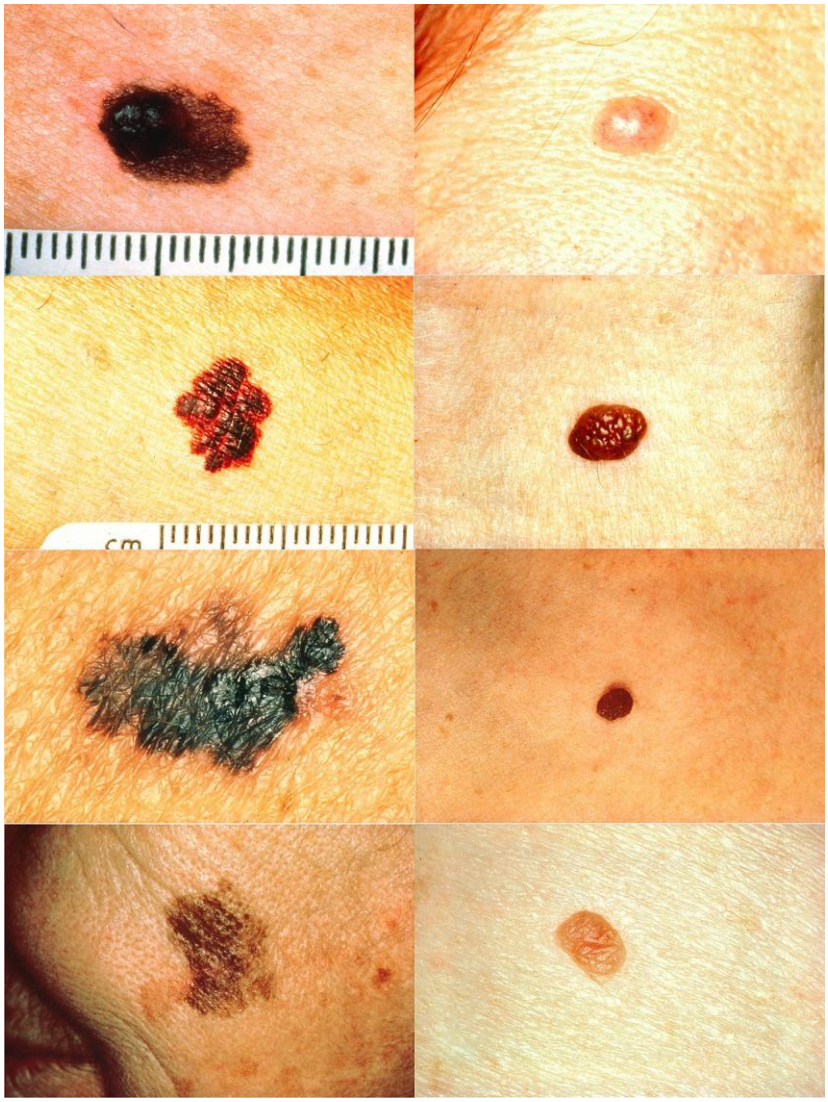
More aggressive Common in Middle age men

Sharply demarcated, blue-black papules 1-2cm.Usually trunk.Middle age men

Increased vertical growth than radial phase.

Lack horizontal growth phase





CA BREAST

It is the second most common cancer in women in India.

PREDISPOSING FACTORS are

Genetic

BRCA1, BRCA2, P53, HNPCC, AT

Hormonal factors : Early menarche, late menopause, hormone replacement therapy (> 10 years), nulliparity, Late first birth

Familial

- First-degree relative with breast cancer under 40 years old
- Two first-degree relatives with breast cancer under 60 years
- Three first-degree relatives with breast cancer at any age
- First-degree relative with breast and ovarian cancer
- First-degree relative with bilateral breast cancer

Histological types

The majority (85%) of breast cancer is ***Invasive Ductal Cancer***.

Ductalcarcinoma can be graded from 1 to 3

Grade 1- well differentiated, low grade

Grade 2 – Moderately differentiated

Grade 3 - poorly differentiated, high grade on

the basis of a grading system originally described by Bloom and Richardson and modified by Elston and Ellis from Nottingham.

This grading system is based on

- Tubule formation
- Mitotic index
- Differentiation/nuclear pleomorphism

Correlates with tumour outcome.

Lobular carcinoma accounts for about 10% of breastcancers. It is characterized by small round cells infiltratingthe lobule and is often missed on cytology, as the cells can be difficult to differentiatefrom normal epithelial cells .Clinically, lobularcancer tends to be

- Multifocal within the breast
- Bilateral.

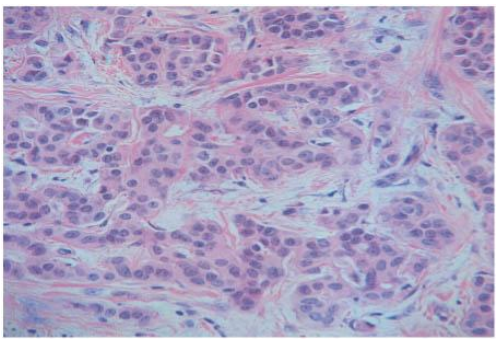
A small percentage of breast cancers belong to special types

- Medullary (lymphocytic infiltration, better prognosis)
- Colloid
- Mucinous,

- Tubular.

Theseare usually towards the well-differentiated end of the spectrum and consequently have a better prognosis.

Invasive ductal carcinoma



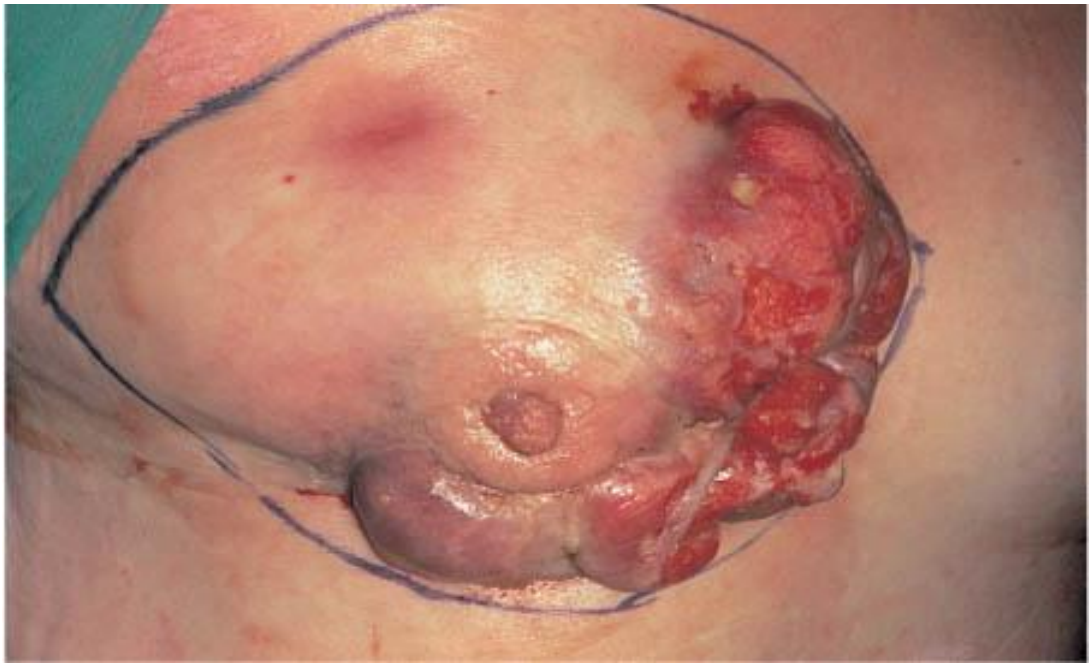
Invasive lobular carcinoma.

Clinical features :

breast lump (in postmenopausal women all new lumps represent malignancy), bloody nipple discharge, skin changes such as tethering or nipple eczema(Paget's disease) , mammographic screening abnormalities.

If neglected breast cancer may ulcerate through the skin of the breast

ULCERATIVE LESION OF BREAST:



Triple assessment.

- ***Physical examination***
- ***Radiological assessment***
    - Ultrasound in patients under 35 years old
    - Mammography in patients over 35 years old
- ***Pathological assessment***

Fine-needle aspiration cytology

The cells are classified as follows:

Cl, inadequate

C2normal/benign

C3, atypia probably benign

C4, atypia probably malignant;

C5, malignant

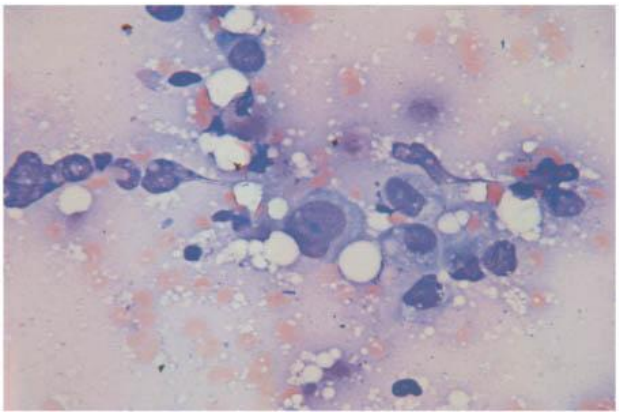
When cytology is unhelpful the next step

- Trucut biopsy

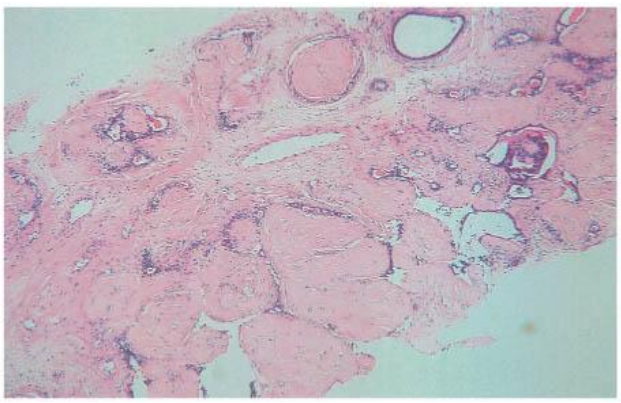
Advantages over FNAC :

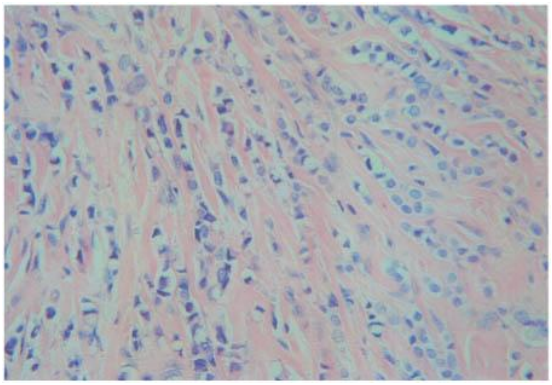
If a lump is malignant, Histological assessment of tumour grade oestrogen receptorstatus can also be assessed

MALIGNANT CYTOLOGY:



Core biopsy histology showing IDC:





TNM classification

Primary Tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Tis (DCIS)	Ductal carcinoma in situ
Tis (LCIS)	Lobular carcinoma in situ
Tis (Paget's)	Paget's disease of the nipple not associated with invasive carcinoma or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma.
T1	Tumor ≤20 mm in greatest dimension
T1mi	Tumor ≤1 mm in greatest dimension
T1a	Tumor >1 mm but ≤5 mm in greatest dimension
T1b	Tumor >5 mm but ≤10 mm in greatest dimension
T1c	Tumor >10 mm but ≤20 mm in greatest dimension
T2	Tumor >20 mm but ≤50 mm in greatest dimension
T3	Tumor >50 mm in greatest dimension
T4	Tumor of any size with direct extension to the chest wall and/or to the skin
T4a	Extension to the chest wall, not including only pectoralis muscle adherence or invasion
T4b	Ulceration and/or ipsilateral satellite nodules and/or edema of the skin
T4c	Both T4a and T4b
T4d	Inflammatory carcinoma

Regional Lymph Nodes (N)	
pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN0(i–)	No regional lymph node metastasis histologically, negative IHC
pN0(i+)	Malignant cells in regional lymph node(s) no greater than 0.2 mm
pN0(mol–)	No regional lymph node metastasis histologically, negative molecular findings (IHC)
pN0(mol+)	Positive molecular findings (RT-PCR), but no metastasis detected by histology or IHC
pN1	Micrometastases; or metastases in one to three axillary nodes; and/or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected
pN1mi	Micrometastases (>0.2 mm and/or >200 cells but none >2.0 mm)
pN1a	Metastases in one to three axillary nodes; at least one metastasis >2.0 mm
pN1b	Metastases in internal mammary nodes with micrometastasis or macrometastases detected by sentinel lymph node biopsy (not clinically detected)
pN1c	Metastases in one to three axillary nodes and in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected
pN2	Metastases in four to nine axillary nodes; or in clinically detected internal mammary lymph nodes in the absence of axillary lymph node metastases
pN2a	Metastases in four to nine axillary nodes (at least one tumor deposit >2.0 mm)
pN2b	Metastases in clinically detected internal mammary lymph nodes in the absence of axillary lymph node metastases
pN3	Metastases in ten or more axillary nodes; or in infraclavicular (level III axillary nodes); or in clinically detected ipsilateral internal mammary lymph nodes in the presence of one or more positive level I, II axillary nodes; or in more than three axillary lymph nodes and internal mammary lymph nodes, with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected; or in ipsilateral supraclavicular lymph nodes
Distant Metastases (M)	
M0	No clinical or radiographic evidence of distant metastases
cM0(i+)	No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumor cells in circulating blood, bone marrow, or other nonregional nodal tissue that are no larger than 0.2 mm in a patient without symptoms or signs of metastases
M1	Distant detectable metastases as determined by classic clinical and radiographic means and/or histologically proven larger than 0.2 mm

MANAGEMENT :

I. Surgery

II. Radiotherapy

III. Hormone Therapy

IV. Chemotherapy

- Multi-pronged approach adopted

SURGICAL APPROACH consists of

MASTECTOMY is indicated for large tumours (in relation to the size of the breast), central tumours beneath or involving the nipple, multifocal disease, local recurrence or patient preference. The radical Halsted mastectomy, which included excision of the breast, axillary lymph nodes and pectoralis major and minor muscles, is no longer indicated as it causes excessive morbidity with no survival benefit. The modified radical (Patey) mastectomy is more commonly performed and is thus described below.

Simple mastectomy involves removal of only the breast with no dissection of the axilla, except for the region of the axillary tail of the breast, which usually has attached to it a few nodes low in the anterior group.

PATEY MASTECTOMY

The breast and associated structures are dissected *en bloc* and the excised mass is composed of :

• the whole breast;

• a large portion of skin, the centre of which overlies the tumour but which always includes the nipple;

• all of the fat, fascia and lymph nodes of the axilla.

The pectoralis minor muscle is either divided or retracted to gain access to the upper two-thirds of the axilla. The axillary vein and nerves to the serratus anterior and latissimus dorsi (the thoracodorsal trunk) should be preserved. The intercostal brachial nerves are usually divided in this operation and the patient should be warned about sensation changes postoperatively. The wound is drained using a wide-bore suction tube. Early mobilisation of the arm is encouraged and physiotherapy helps normal function to return very quickly; most patients are able to resume light work or housework within a few weeks.

CONSERVATIVE BREAST CANCER SURGERY

This is aimed at removing the tumour plus a rim of at least 1 cm of normal breast tissue. This is commonly referred to as a wide local excision. The term lumpectomy should be reserved for an operation in which a benign tumour is excised and in which a large amount of normal breast tissue is not resected. A quadrantectomy involves removing the entire segment of the breast that contains the tumour. Both of these operations are usually combined with axillary surgery, usually via a separate incision in the axilla. There are various options that can be used to deal with the axilla, including sentinel node biopsy, sampling, removal of the nodes behind and lateral to the pectoralis minor (level II) or a full axillary dissection (level III).

There is a somewhat higher rate of local recurrence following conservative surgery, even if combined with radiotherapy, but the long-term outlook in terms of survival is unchanged. Local recurrence is more common in younger women and in those with high-grade tumours and involved resection margins. Patients whose margins are involved should have a further local excision (or a mastectomy) before going on to radiotherapy. Excision of a breast cancer without radiotherapy leads to an unacceptable local recurrence rate.

The role of axillary surgery is to stage the patient and to treat the axilla. The presence of metastatic disease within the axillary lymph nodes remains the best single marker for prognosis; however, treatment of the axilla does not affect

long-term survival, suggesting that the axillary nodes act not as a ‘reservoir’ for disease but as a marker for metastatic potential. It used to be accepted that only premenopausal women should have their axilla staged by operation as there was a good case for giving chemotherapy to lymph node-positive patients; however, it is now clear that postmenopausal women also benefit from chemotherapy and so all patients require axillary surgery. In postmenopausal patients, tamoxifen was once given regardless of axillary lymph node status, but it is now known that only hormone receptor-positive patients, irrespective of age, benefit from this. Axillary surgery should not be combined with radiotherapy to the axilla because of excess morbidity. Removal of the internal mammary lymph nodes is unnecessary.

SENTINEL NODE BIOPSY

This technique has become the standard of care in the management of the axilla in patients with clinically node-negative disease. The sentinel node is localised peroperatively by the injection of patent blue dye and radioisotope labelled albumin in the breast. The recommended site of injection is in the subdermal plexus around the nipple although some still inject on the axillary side of the cancer. The marker passes to the primary node draining the area and is detected visually and with a hand-held gamma camera. Peropererative diagnosis allows completion axillary clearance if nodal disease is detected. This may be achieved

with frozen-section analysis, touch imprint cytology (TIC) or by molecular methods. These involve homogenising the node and detection of a gene such as cytokeratin 19 or mammoglobin. In some cases there are only subcapsular micrometastases that are missed at frozen section. In patients in whom there is no tumour involvement of the sentinel node, further axillary dissection can be avoided. A nomogram outlining the chances of further axillary node positivity has been developed by the group at Memorial Sloan Kettering Hospital, New York. Recent trial results have called into question the utility of completion axillary clearance after a positive sentinel node has been detected but, at present, this remains controversial.

RADIOTHERAPY

Radiotherapy to the chest wall after mastectomy is indicated in selected patients in whom the risks of local recurrence are high. This includes patients with large tumours and those with large numbers of positive nodes or extensive lymphovascular invasion. There is some evidence that postoperative chest wall radiotherapy improves survival in women with node-positive breast cancer. It is conventional to combine conservative surgery with radiotherapy to the remaining breast tissue. Recurrence rates are too high for treatment by local excision alone except in special cases (small node-negative tumours of a special type). Trials are under way to investigate whether radiotherapy can be given intraoperatively at one sitting or as an accelerated postoperative course. This

would have considerable advantages in making conservative surgery available in areas where radiotherapy is not currently used. It would also relieve the burden of the current demand for radiotherapy, which accounts for up to 40 per cent of activity in some departments.

CHEMOTHERAPY

Chemotherapy using a first-generation regimen such as a six monthly cycle of cyclophosphamide, methotrexate and 5-fluorouracil (CMF) will achieve a 25 per cent reduction in the risk of relapse over a 10- to 15-year period. It is important to understand that this 25 per cent reduction refers to the likelihood of an event happening. For example, a woman with a 96 per cent chance of survival at, say, five years only has a 4 per cent chance of death over this time and the absolute benefit from chemotherapy would be an increase in survival rate of 1 per cent, to 97 per cent. This would not be a sufficient gain to offset the side effects of this potentially toxic therapy. However, for a woman with a 60 per cent chance of dying (40 per cent survival rate) a 25 per cent reduction in risk would increase her likelihood of survival to 55 per cent and thus treatment would be worthwhile. CMF is no longer considered adequate adjuvant chemotherapy and modern regimens include an anthracycline (doxorubicin or epirubicin) and the newer agents such as the taxanes.

Chemotherapy was once confined to premenopausal women with a poor prognosis (in whom its effects are likely to be the result, in part, of a chemical castration effect) but is being increasingly offered to postmenopausal women with poor prognosis disease as well. Chemotherapy may be considered in patients if other prognostic factors, such as tumour grade, imply a high risk of recurrence. The effect of combining hormone and chemotherapy is additive although hormone therapy is started after completion of chemotherapy to reduce side effects. High-dose chemotherapy with stem cell rescue for patients with heavy lymph node involvement has now been shown in controlled trials to offer no advantage and has been abandoned.

Primary chemotherapy (neoadjuvant) is being used in many centres for large but operable tumours that would traditionally require a mastectomy (and almost certainly postoperative adjuvant chemotherapy). The aim of this treatment is to shrink the tumour to enable breast-conserving surgery to be performed. This approach is successful in up to 80 per cent of cases but is not associated with improvements in survival compared with conventionally timed chemotherapy. For older patients with breast cancers strongly positive for hormone receptors a similar effect can be seen with three months of endocrine treatment.

Newer ‘biological’ agents will be used more frequently as molecular targets are identified – the first of these, trastuzamab (Herceptin), is active against tumours

containing the growth factor receptor c-erbB2. Other agents currently available include bevacizumab, a vascular growth factor receptor inhibitor, and lapitinab, an oral combined growth factor receptor inhibitor.

CA RECTUM AND ANAL CANAL :

Adenocarcinoma of the colon and rectum is one of the most common cancers occurring in the western world. It occurs in both sexes but morecommon in men. Almost half of these tumours occur inthe rectum and almost three-quarters are within reach of the flexible sigmoidoscope (60 cm from the anal margin).

Pathology

Carcinoma of the colon or rectum is an adenocarcinoma with a fibrous stroma that may progress in different ways:

• as an exophytic cauliflower-type of growth;
• as an ulcerating lesion penetrating through the bowel wall;
• as an annular constricting growth;
• as a diffuse infiltrating tumour;
• as the rare colloidal mucus-secreting tumour.

Colorectal carcinoma metastasizes to regional lymph nodes and via the bloodstream to the liver.

OBSERVATION

A total of 50 patients with clinically evident surface malignancies were studied. Out of the 50, 46 lesions proved to be malignant and 4 were benign.
All lesions of the oral cavity were correctly diagnosed by scrape/imprint method.

There were 5 cases of Ca Rectum of which 2 were misinterpreted as benign by scrape/imprint method while biopsy turned out to be Adenocarcinoma and 1 was benign lesion by all the three methods and two cases were malignant by all the three methods.

There were 12 cases of cutaneous ulcers of which 2 were Benign and 10 were malignant by biopsy. But out of the 10 lesions, 1 lesion was misinterpreted as inflammatory by cytology but was proven by biopsy as SCC.

1 case of Soft tissue sarcoma Lt arm was proven by HPE as Pleomorphic Sarcoma but misdiagnosed as benign by scrape/imprint cytology.

Out of the 6 Ca Breast cases, one biopsy proven Invasive Ductal Carcinoma was missed by cytology.

2 cases of Secondaries neck were studied of which 1 biopsy proven inflammatory lesion was misinterpreted by imprint cytology as malignant, while scrape cytology showed no evidence of malignancy.

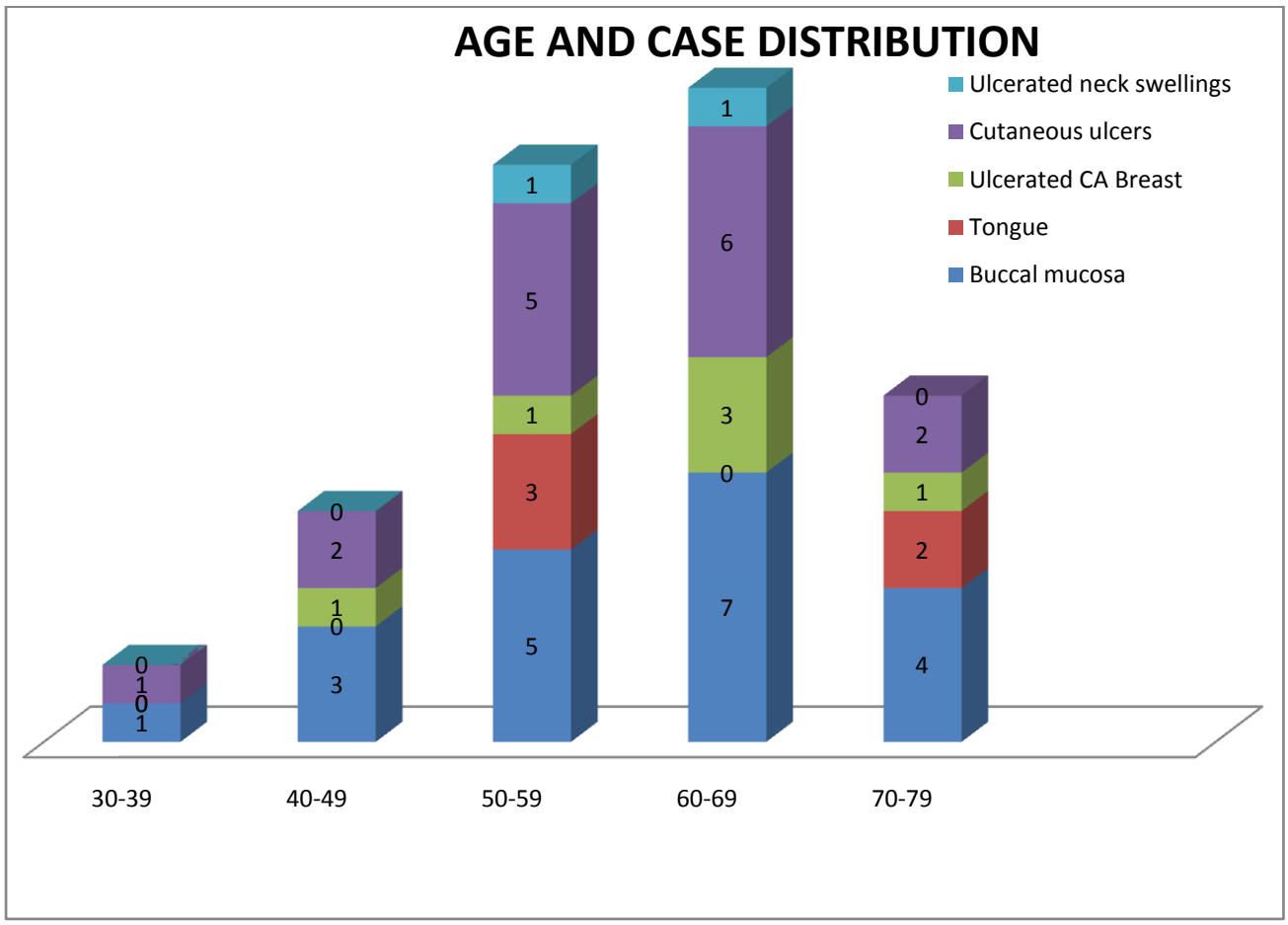
There was discordance in biopsy proven 4 cases between imprint and scrape cytology of which 3 were cases of Ca oral cavity SCC shown to be dysplasia by Imprint but malignant cells positive by Scrape cytology and 1 case of Ca Breast IDC was reported as inflammatory in Imprint, malignancy by scrape cytology.

Among 50 cases, histological subtypes were conclusive by either of the cytological methods in 43 cases.

Scrape cytology was found to be more useful for ulcerative lesions.

AGE DISTRIBUTION

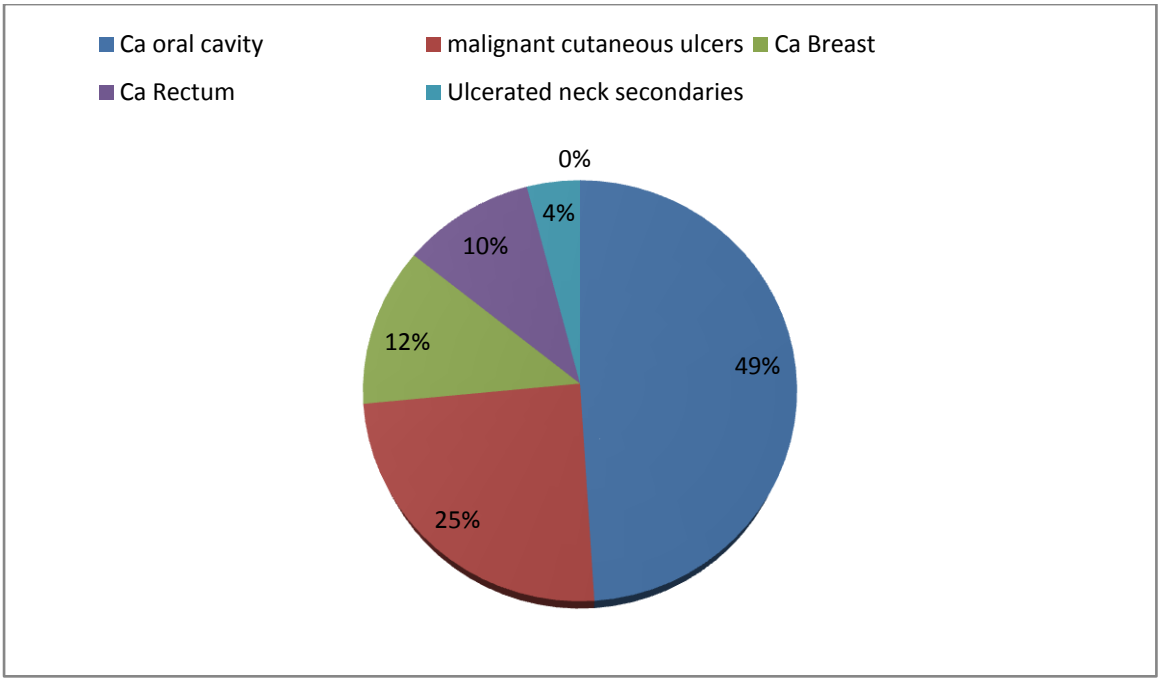
Age	**Frequency**	**Percentage**
Below 40yrs	3	6.0
41 to 50yrs	9	18.0
51 to 60yrs	17	34.0
61 to 70yrs	13	26.0
71 to 80yrs	8	16.0
Total	50	100.0



Number indicates number of patients affected by the disease

CASE DISTRIBUTION

LESION	No. of cases	Malignant	Benign	False positive	False negati
Ca Oral cavity	24	24	-	-	-
Malignant Cutaneous ulcers	12	10	2	-	1
Ca Breast	6	6	-	-	1
Ca Rectum	5	4	1	-	1
Ulcerated neck swellings	2	1	1	1	-
Soft tissue sarcoma	1	1	-	-	1
TOTAL	50	46	4	1	4



	DISEASED	**NON DISEASED**	**TOTAL**
TEST POSITIVE	42	1	43
TEST NEGATIVE	4	3	7
TOTAL	46	4	50

SENSITIVITY

The sensitivity of a clinical test refers to the ability of the test to correctly identify those patients with the disease(True positives)

Sensitivity of scrape/imprint cytology by this study – 91%

SPECIFICITY

The specificity of a clinical test refers to the ability of the test to correctly identify those patients without the disease(True negatives)

Specificity of scrape/imprint cytology by this study – 75%

SENSITIVITY	91%
SPECIFICITY	75%
POSITIVE PREDICTIVE VALUE	97%
NEGATIVE PREDICTIVE VALUE	43%

TOTAL CASES	CASES DETECTED BY IMPRINT CYTOLOGY	CASES DETECTED BY SCRAPE CYTOLOGY	BIOPSY
MALIGNANT - 46	43	42	46
BENIGN - 4	3	2	4

RESULTS

A total of 50 patients with clinically evident Surface malignancies were studied. Out of the 50, 46 lesions proved to be malignant and 4 were benign. All lesions of the oral cavity were correctly diagnosed by scrape/imprint method.

There were 5 cases of Ca Rectum of which 2 were misinterpreted as benign by scrape/imprint method while biopsy turned out to be Adenocarcinoma and 1 was benign lesion by all the three methods.

There were 12 cases of Malignant cutaneous ulcers of which 2 were Benign and 10 malignant of which 1 lesion was misinterpreted as inflammatory but was proven by biopsy as SCC.

1 case of Soft tissue sarcoma Lt arm was proven by HPE as Pleomorphic Sarcoma but misdiagnosed as benign by scrape/imprint cytology.
Out of the 6 Ca Breast cases,1 biopsy proven Invasive Ductal Carcinoma was missed by cytology.

2 cases of ulcerated neck swellings were studied of which 1 biopsy proven inflammatory lesion was misinterpreted by imprint cytology as malignant, while scrape cytology showed no evidence of malignancy.

There was discordance in 4 cases between imprint and scrape cytology of which 3 were cases of Ca oral cavity SCC shown to be dysplasia by Imprint but malignant cells positive by Scrape cytology and 1 case of Ca Breast IDC was reported as Benign in Imprint, malignancy by scrape cytology. Among 50 cases, histological subtype was conclusive by either of the cytological methods in 43 cases.

Scrape cytology was found to be more useful for ulcerative lesions.

Totally there were 1 false positive and 4 false negative result.
In 86% of cases exact cytopathological diagnosis was reached which correlated with HPE diagnosis.

DISCUSSION

During the one year study period, 50 cases were examined of which 46 were malignant i.e. 92%. Most common malignancy is oral cavity malignancy with males preponderance, followed by malignant cutaneous ulcers.

In oral malignancies out of the 26 cases studied, predominant were Ca – buccal mucosa , owing to the common etiological factor – Tobacco chewing. Among 3 biopsy proven cases of oral malignancies, imprint cytology reveals dysplasia but scrape cytology shows positive malignant cells. But by either one of the methods, the cytological diagnosis matched HPE results in all the cases. Hence in this study it is observed that establishing cytological diagnosis is more accurate in cases of oral malignancies.

There were 12 cases of malignant cutaneous ulcers of which 2 were Benign and 10 were malignant. Out of which 1 lesion was misinterpreted as benign but was proven by biopsy as SCC. The commonest lesion that presented as malignant cutaneous ulcer was SCC Followed by malignant melanoma.

Of the 6 biopsy proven Ca breast cases studied, 1 case was found to be benign by cytology. One discordance was observed between imprint

[inflammatory] and scrape [malignancy] cytology. Exact cyto-pathological diagnosis was made in half the cases.

Of the 5 Ca rectum and anal canal cases studied, 2 cases were found to be malignant by all three methods. 3 cases were benign by cytology. Out of those 3 cases, 2 turned out to be malignant by biopsy. 1 case was benign by all three methods. Cytological methods seem to be less helpful in the diagnosis of ca rectum.

One case of pleomorphic sarcoma was misinterpreted as benign this shows that malignancies with excessive stromal components, cytology is inconclusive

CONCLUSION

- Scrape/Imprint cytology is a rapid, safe, simple & inexpensive method to diagnose suspicious malignant lesion.
- If scrape / imprint is positive, we can proceed with next level of management (surgery if needed) without waiting for biopsy report.
- It can be done in resource poor conditions and promote early diagnosis and referral to specialist care.
- Allays anxiety due to shorter waiting period and aids in quick decision making.
- Highly sensitive, hence can be used as a rapid screening test.
- Comparable to HPE reports in 86% of cases, hence can be used as valuable tool in PHCs & district hospitals
- Minimal cellular distortion provides crisp cytological details.

LIST OF ABBREVIATIONS USED

SCC	Squamous Cell Carcinoma
AC	Adenocarcinoma
MM	Malignant Melanoma
AM	Amelanocytic Melanoma
PS	Pleomorphic Sarcoma
STS	Soft Tissue Sarcoma
IDC	Invasive Ductal Carcinoma
MAL	Smear positive for malignancy
INF	Inflammatory cells
NEM	No Evidence of Malignancy
BEN	Benign
DYS	Dysplasia

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	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1	S.NO	NAME		AGE	SEX	CLINICAL DIAGNOSIS			IMPRINT CYTOLOGY		SCRAPE CYTOLOGY		BIOPSY	
2	1	ALAGESAN		49	M	SCC Left Foot			SCC		SCC		SCC	
3	2	BASKAR		50	M	Ca Rectum			INF		INF		AC	
4	3	SUNDAR		39	M	Ca Buccal mucosa			SCC		SCC		SCC	
5	4	SIVAGNANAM		47	M	Ca Rectum/Recurrence			MAL		AC		AC	
6	5	ABUSAMMA		55	F	STS Left arm/Recurrence			Spindle cell lesion		inadequate		PS	
7	6	VENKATACHALAM		80	M	Ca Lower Lip			SCC		SCC		SCC	
8	7	CHITRAVEL		50	M	Growth Lt Index finger			SCC		SCC		SCC	
9	8	AMUTHA		50	F	Ca Lt Breast			MAL		IDC		IDC	
10	9	THIRUNAVUKKARASU		55	M	SCC Left Foot			INF		INF		SCC	
11	10	AMBIKA		33	F	Ca Rectum			?POLYP/BEN		INF		AC	
12	11	AROKIYA MARY		60	F	Ca Rt Breast			INF		MAL		IDC	
13	12	VELLAIYAMMAL		60	F	Ca Lt Breast			IDC		IDC		IDC	
14	13	PERAMAIYAN		70	M	AM Lt Arm			MM		MM		CARCINOSARCOMA	
15	14	ANANDH		55	M	Ca Lip			MAL		MAL		SCC	
16	15	KATHAVARAYAN		56	M	Ca Lt Buccal mucosa			MAL		MAL		SCC	
17	16	SEKAR		55	M	Ca Lip			MAL		MAL		SCC	
18	17	RAJAMANIKAM		64	M	SCC Rt Foot			MAL		SCC		SCC	
19	18	CHINNAPILLAI		55	M	Ca Rt Buccal mucosa			DYS		MAL		SCC	
20	19	PANNEERSELVAM		45	M	Ca Rt Buccal mucosa			DYS		SCC		SCC	
21	20	PERIYASAMY		50	M	Ca Rt Buccal mucosa			SCC		MAL		SCC	
22	21	JAYARAMAN		63	M	Ca Rt Buccal mucosa			DYS		SCC		SCC	
23	22	KALIYAMOORTHY		72	M	MM Rt Foot			MAL		MAL		MM	
24	23	DHANISHILESH		65	M	Ca Lt Buccal mucosa			SCC		SCC		SCC	
25	24	JEYARAMAN		65	M	Ca Rt Buccal mucosa			SCC		SCC		SCC	
26	25	SUBRAMANIAN		75	M	Ca Rt RMT			DYS		SCC		SCC	
27	26	PAKKIYAM		70	F	Ca Lower Lip			SCC		SCC		SCC	
28	27	MALARKODI		55	F	Ca Lip			MAL		SCC		SCC	
29	28	RAJENDRAN		52	M	Secondaries neck			SCC		INF		SCC	
30	29	RAMANATHAN		61	M	Ca Rectum			AC		AC		AC	
31	30	MURUGESAN		71	M	Ca Lower Lip			SCC		SCC		SCC	
32	31	RATHINASAMY		67	M	Marjolins Ulcer			BEN		INF		INF	
33	32	PARVATHI		60	F	Ca Rt Buccal mucosa			SCC		SCC		SCC	
34	33	RAMANATHAN		62	M	Ca Rt Buccal mucosa			SCC		MAL		SCC	
35	34	DURAIYAPPAN		62	M	MM Lt Foot			MAL		MAL		MM	
36	35	SIVAKUMAR		64	M	Secondaries neck			SCC		INF		INF	
37	36	PERIYAMMA		54	F	Ca Lower Lip			MAL		SCC		SCC	
38	37	ARUNACHALAM		75	M	Ca Lower Lip			SCC		SCC		SCC	
39	38	RAM KUMAR		74	M	Ca RMT			MAL		SCC		SCC	
40	39	RAMAKANNU		62	M	SCC Rt Foot			MAL		SCC		SCC	
41	40	NATARAJAN		65	M	Ca Rt Buccal mucosa			SCC		SCC		SCC	
42	41	RAMASAMY		60	M	Marjolins Ulcer			BEN		INF		ULCER with granulatic	
43	42	GOPAL		58	M	Ca Lt Buccal mucosa			SCC		SCC		SCC	
44	43	KUMUTHA		48	F	Ca Rt Breast			MAL		IDC		IDC	
45	44	RAMAMIRTHAM		72	F	Ca Lt Breast			NEM		NEM		IDC	
46	45	RAJADURAI		46	M	AM Lt Arm			MM		MM		MM	
47	46	SARASWATHI		72	F	Ca Tongue			SCC		SCC		SCC	
48	47	VIJAYALAKSHMI		60	F	Ca Rt Breast			MAL		MAL		IDC	
49	48	KUMARAGURU		52	M	SCC Rt Middle Finger			SCC		SCC		SCC	
50	49	NEDUMARAN		60	M	Ca Rectum			NEM		NEM		NEM	
51	50	NARAYANAN		40	M	Ca Lt Buccal mucosa			SCC		SCC		SCC	

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