Potential application of BEES in Diagnosis of Cancer

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Outline

- Present conventional endoscopic diagnostic tools
- Discuss recent advances allowing targeted biopsies
- Introduce some new diagnostic tests which can be done on scant specimen
- Discuss how Biomorphic explorers (BEES) could explore ‘visceral terrain’ for oncologic diagnosis

Diagnostic Tools in Oncology

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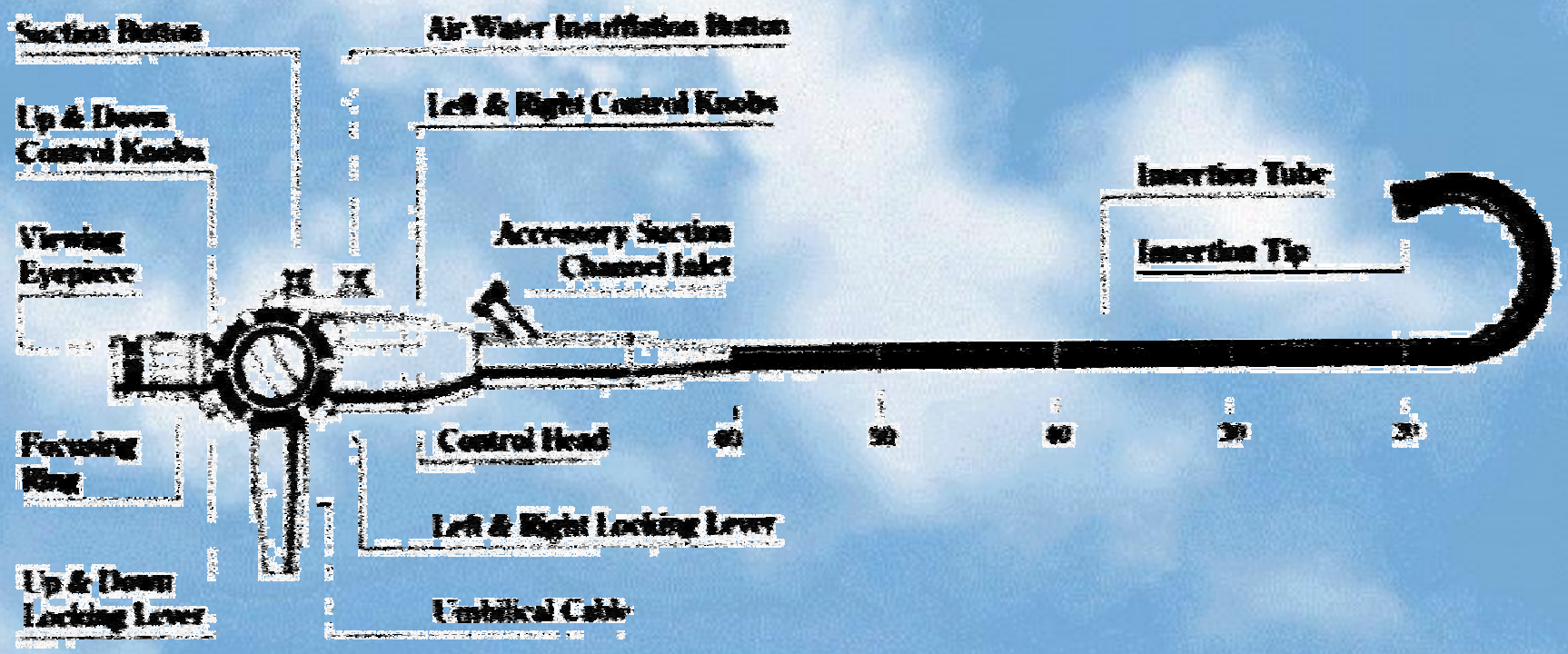
- Cancer presents it self as lump or ‘tumor’, superficially or internally.
- To make a diagnosis, a sample of tissue is required.
- Tissue specimen from superficial lesions can be obtained by percutaneous biopsy.
- If tumor is present on internal lining of viscera, samples may be obtained by endoscopies

Endoscopy

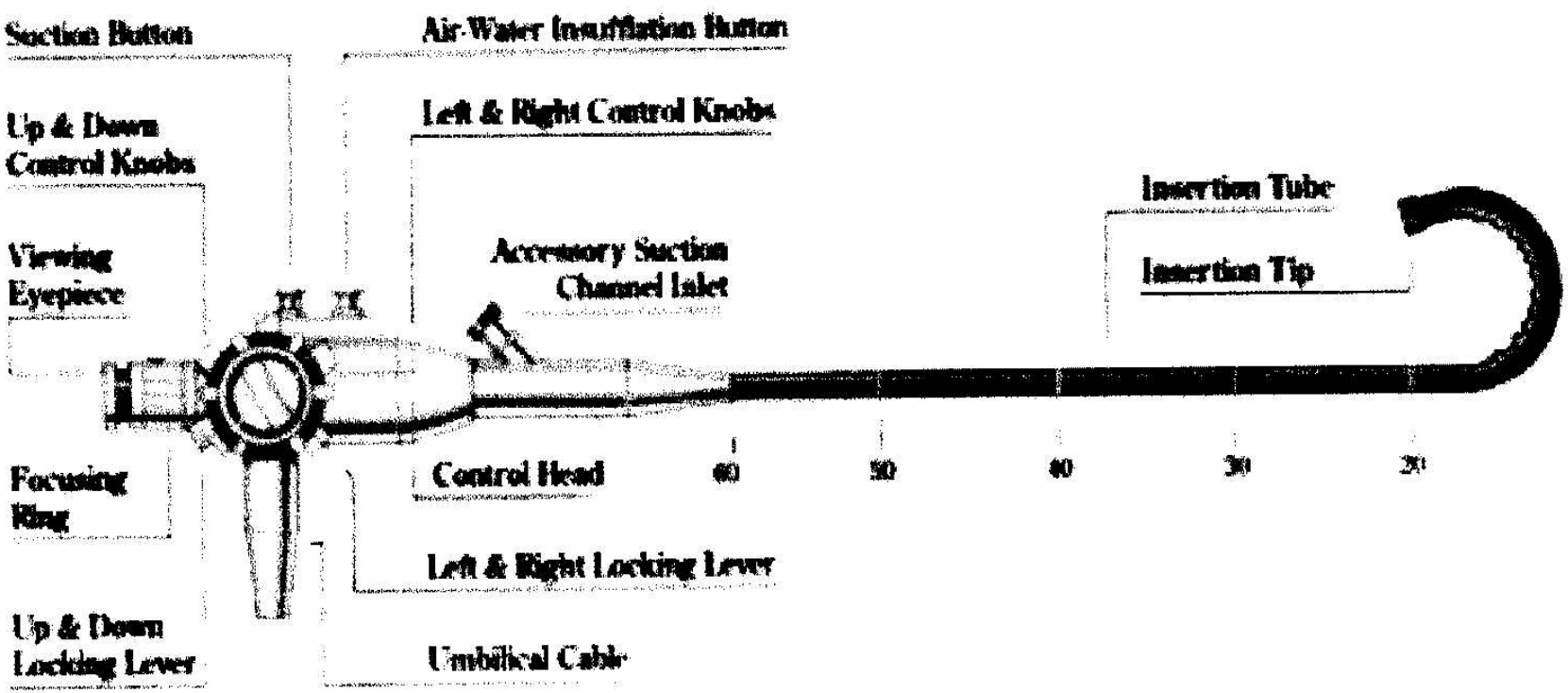
Endoscopy is defined as the procedure to look into body's internal organs using rigid or flexible scopes.

- Nasopharyngoscopy
- Esophago-gastric-duodenoscopy (EGD)
- Bronchoscopy
- Colonoscopy
- Flexible sigmoidoscopy

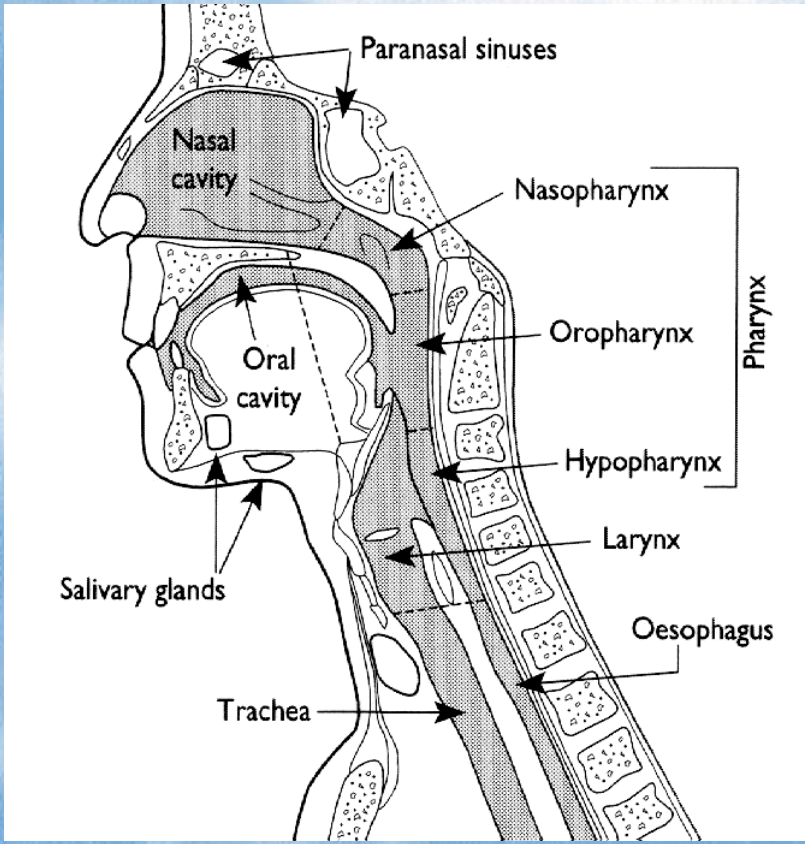
Flexible Endoscope



Flexible Endoscope

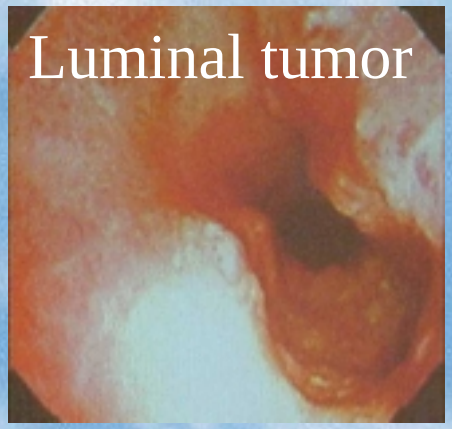


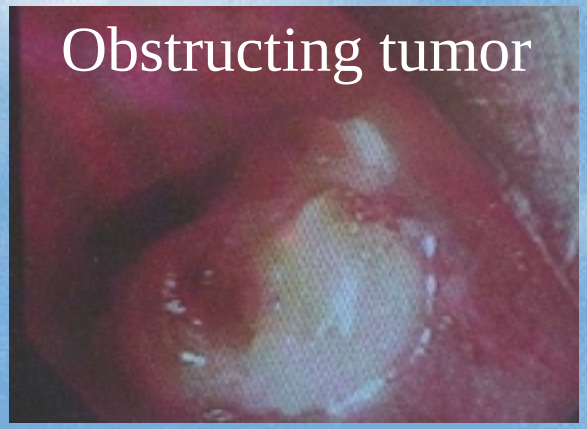
Endoscopy in Diagnostic Oncology



- Visually inspect internal mucosa for abnormalities
- Inspect for abnormal lesions
- Evaluate extent of tumor
- Obtain biopsy specimen

Normal and Abnormal images





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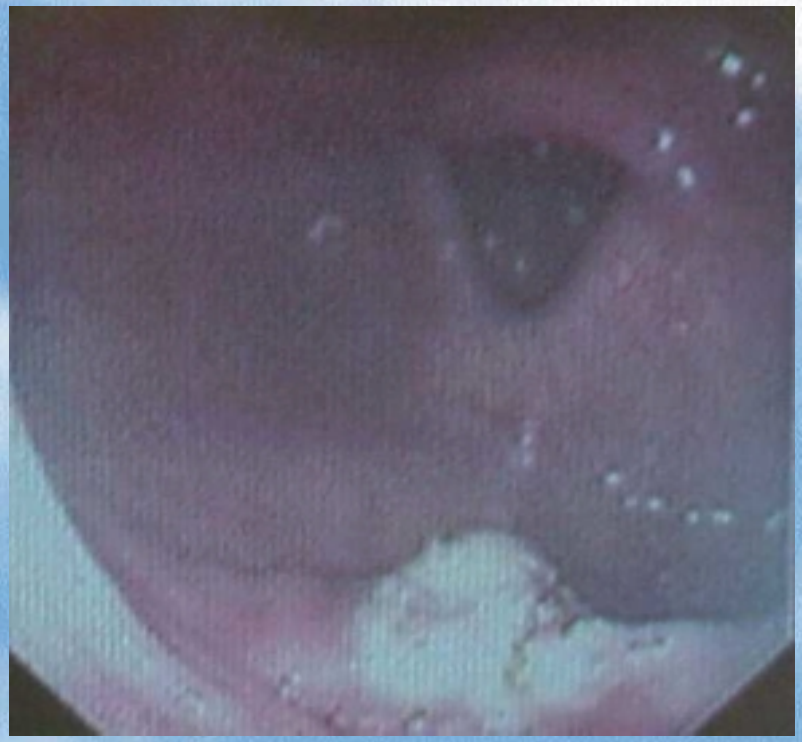
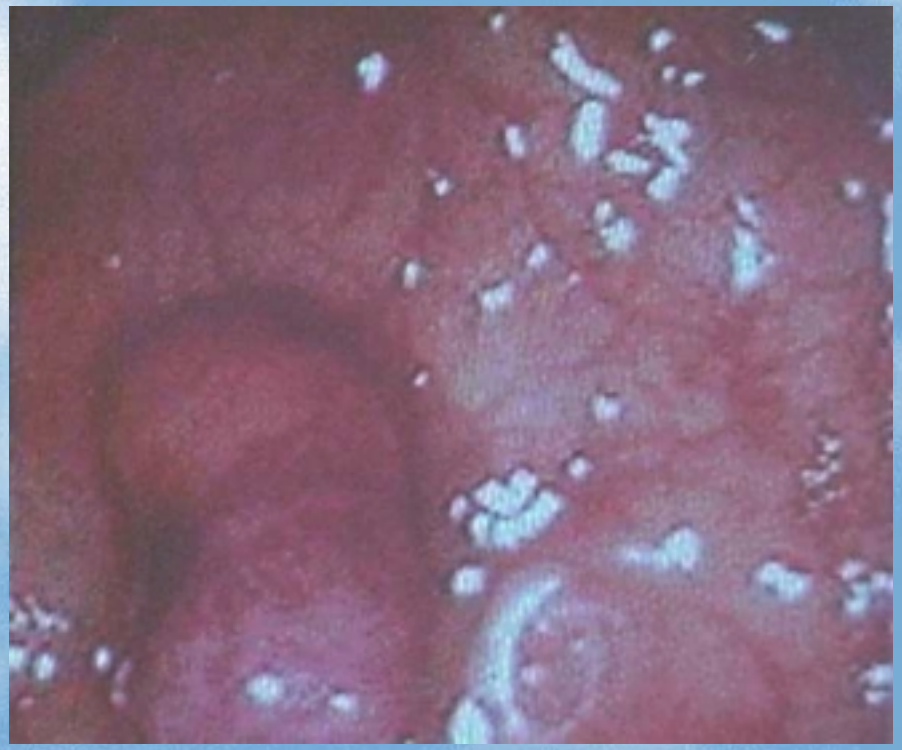
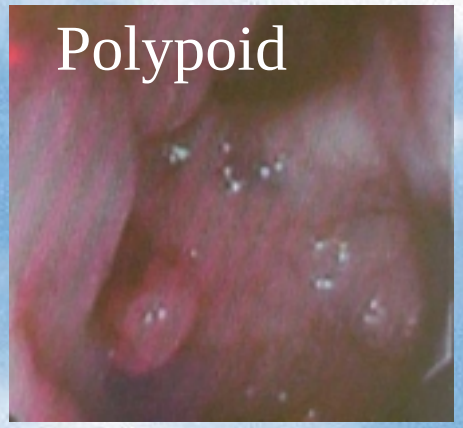
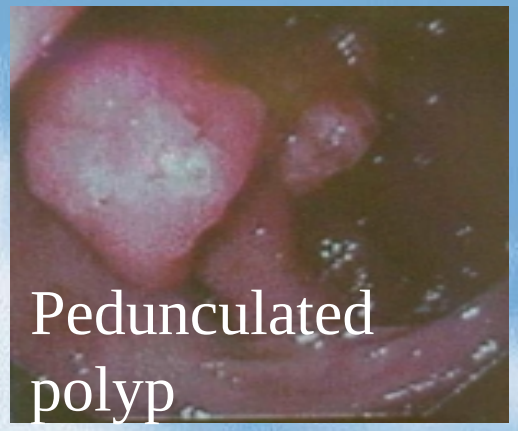
EGD images

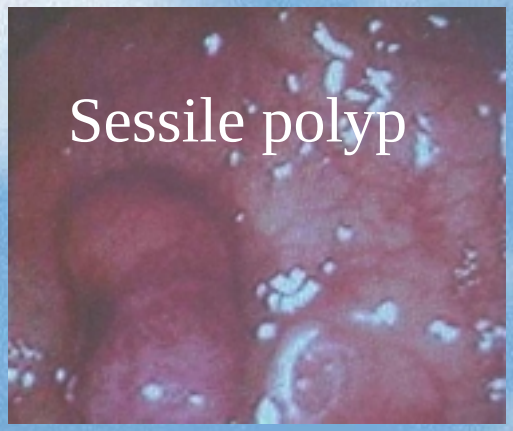




Colonoscopic images







Making a diagnosis after endoscopy

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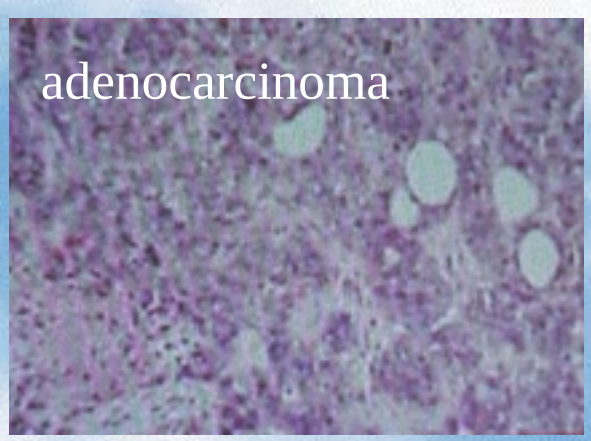
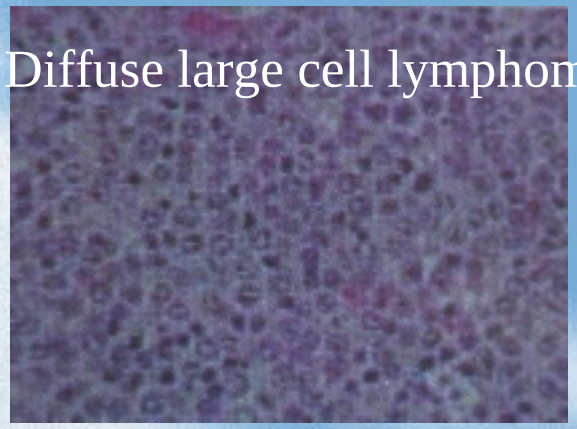
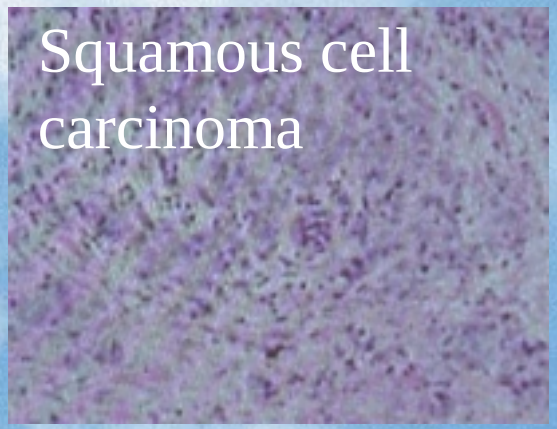
- Submitting a tissue specimen or tissue washing (Broncho-alveolar lavage) for pathology
- Pathologic evaluation using conventional light microscopy
- Applying immunostains and special stains for conclusive diagnosis
- Sophisticated molecular biological tests for diagnosis or prognosis on scant specimen

Pathological specimen

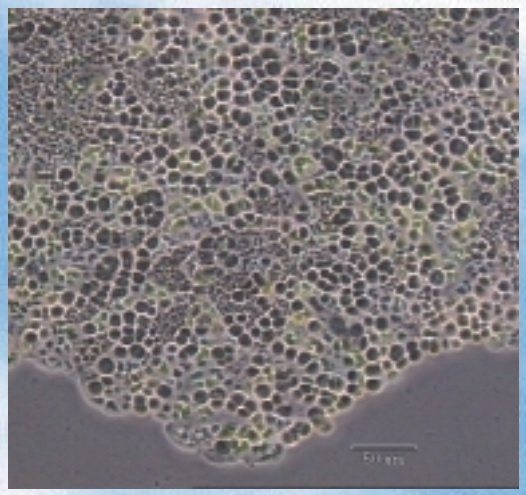


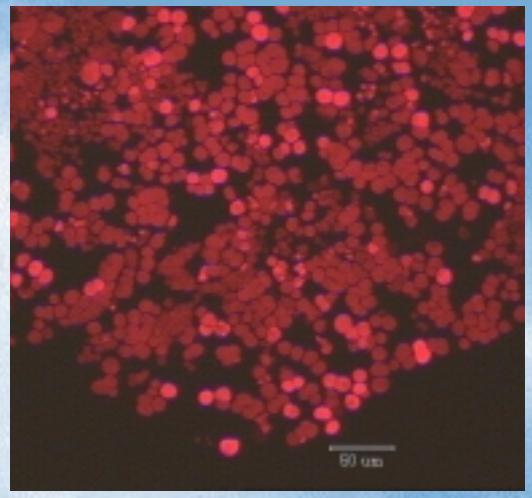




- Pathological diagnosis requires mm to cm size tissue
- Sometimes require multiple procedures as specimen may be inadequate or specimen required for additional tests

Autoflourescence





- Autoflourescence is the ability of some tumor cells to flourescence on exposure to laser light
- Similarly exposure to certain dyes can distinguish difficult to identify cancerous tissue

Specific diagnosis of cancer from small tissue samples

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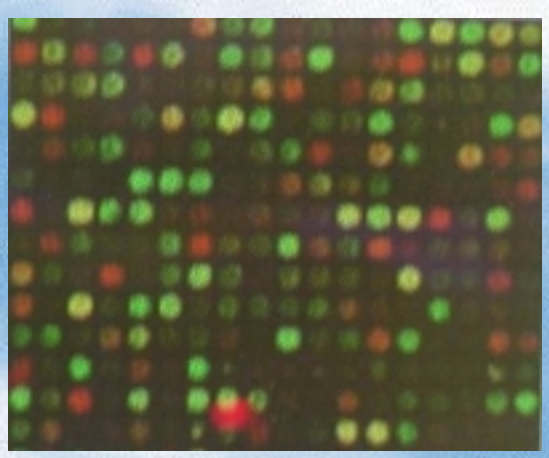
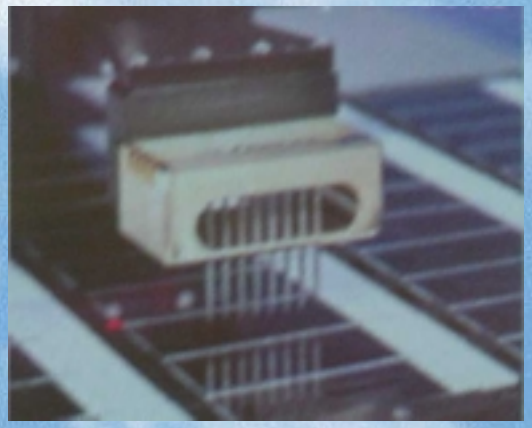
- Identifying key molecular signatures specific to certain cancer
  - **cancer cells may produce a protein or antigen which may be recognized by an antibody, which can be demonstrated by tagging to radioactivity, another enzyme or flourescent molecule (ELISA, FISH, Immunohistochemistry, Flowcytometry etc)**
  - **cancer cells may possess certain known DNA or RNA fragments which can be amplified and detected by PCR or RT-PCR reactions**
- Identifying some enzymes which may be hallmark of malignancy, like telomerase.
- Identifying exact genetic signature of tumors using microarrays or DNA hybridization technology

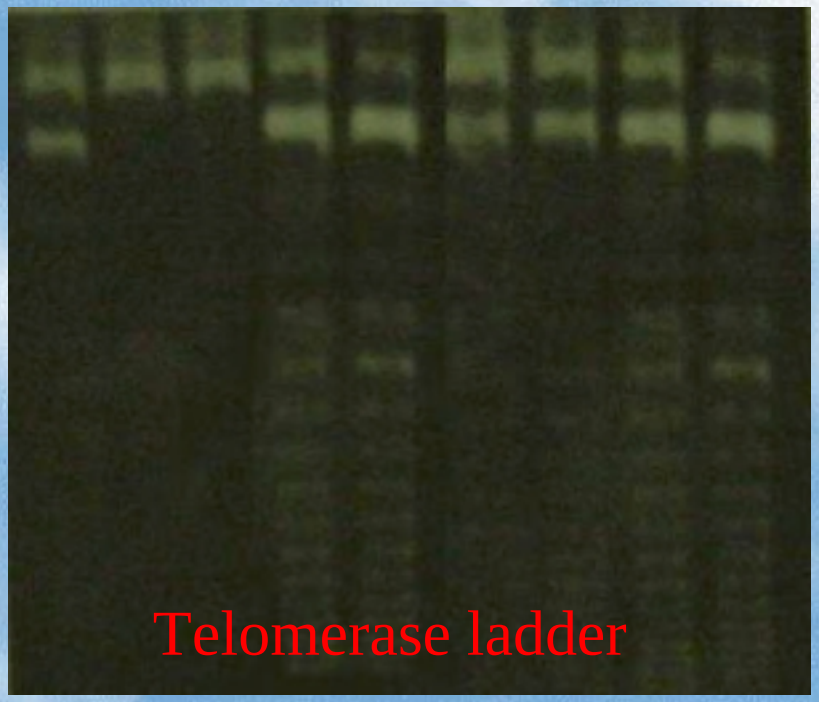
Microarrays





- **DNA from specimen can be broken down into small fragments.**
- **These can be amplified and hybridized with known DNA segments tagged to flourescent dyes**
- **Presence or absence of specific genes can be known in small tumor specimen as a light signal**
- **This information can be used for diagnosis and prognosis**

Telomerase activation



- **Telomeres are tandemly repeated DNA residues at flanks of chromosomes**
- **Telomeres are lost with each successive cell division, and this successive loss leads to senescence**
- **The enzyme telomerase renews the telomerase hence makes the cells immortal**
- **cancer cells usually express telomerase**
- **Activity of this enzyme can be demonstrated by PCR amplification of telomerase products**

Pitfalls of endoscopic diagnosis

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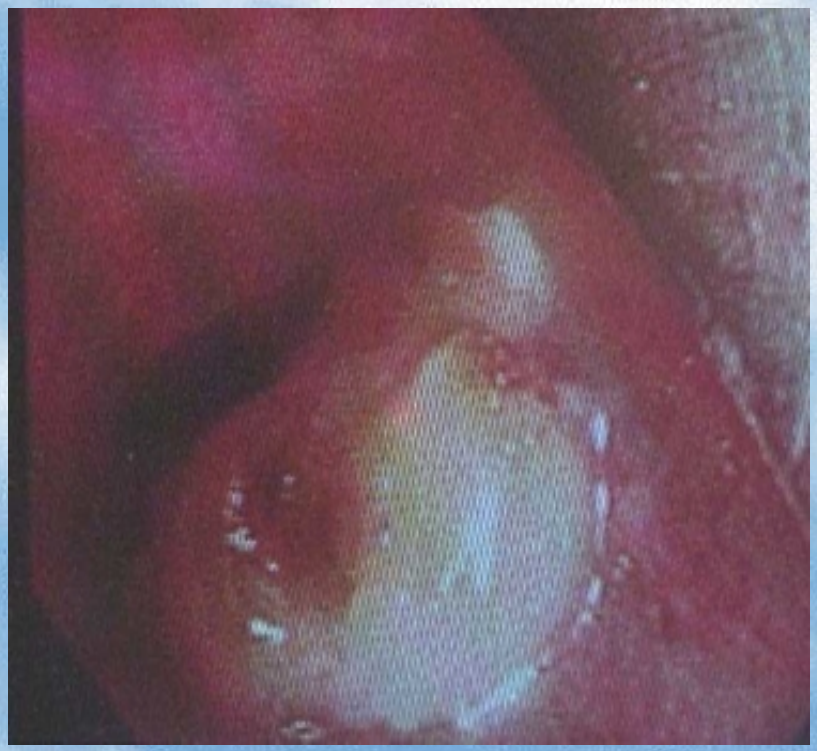
- Bronchoscopy contraindicated in conditions like reactive airway, asthma, cardiac arrythmias.
- Inconveniencing and discomforting to patients
- cannot be performed if intubation not possible, or tumor blocks the passage
- Causes hypoxemia (lack of oxygen), hence not possible in sick patients
- Lots of complications

Complications of Endoscopy

- Hypoxemia
- Perforation
- Aspiration
- Wheezing
- Hypotension
- Bradycardia
- Infection
- Cross contamination

Obstructing lesions



Conceptual design of bioinspired oncologic diagnostic rover

- Diagnostic rovers crawl through nose or mouth or rectum and perform directed travel to target areas.
- Capable of passively travel or have externally controlled movement, using walking parts designed after body flukes.
- Visualize target with wide view camera
- Distinguish cancerous tissue by autoflourescence or external navigation
- Take biopsy using parts fashioned after insect mouth parts.
- Crawl out, pulled back by retractable thread, or pass out of other end.

Bioinspired Endoscopic Rovers

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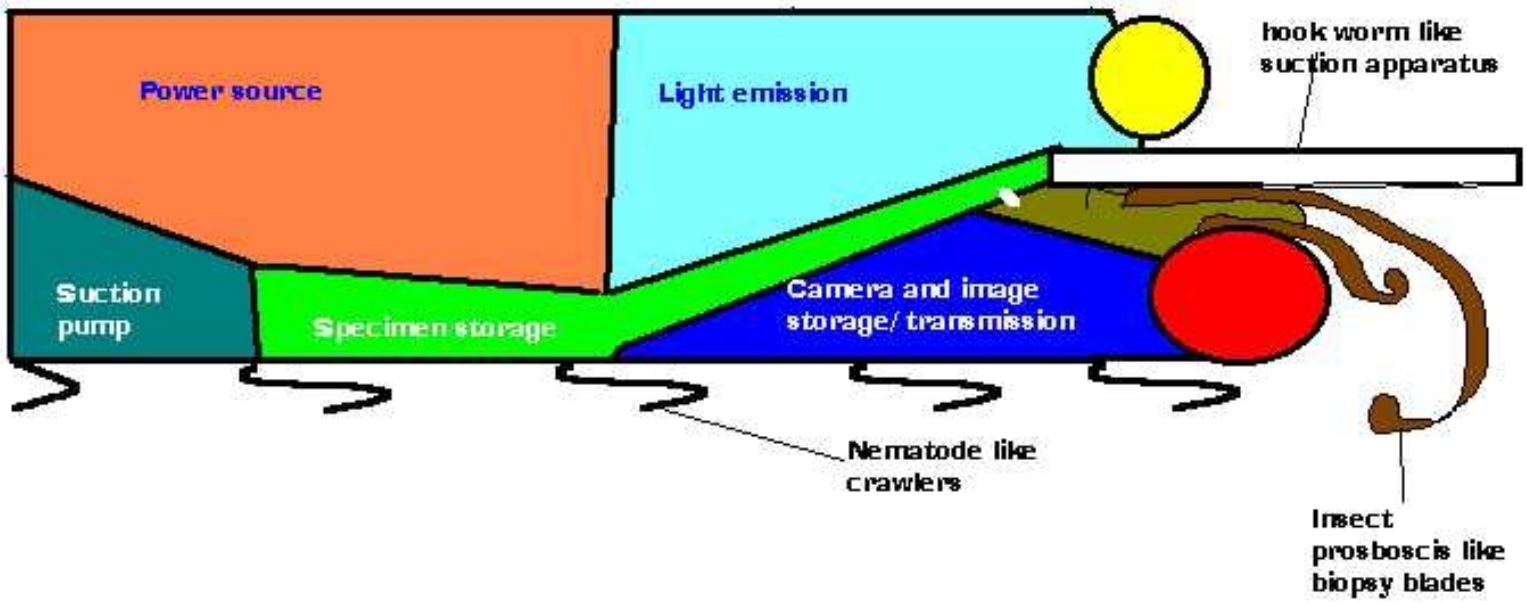
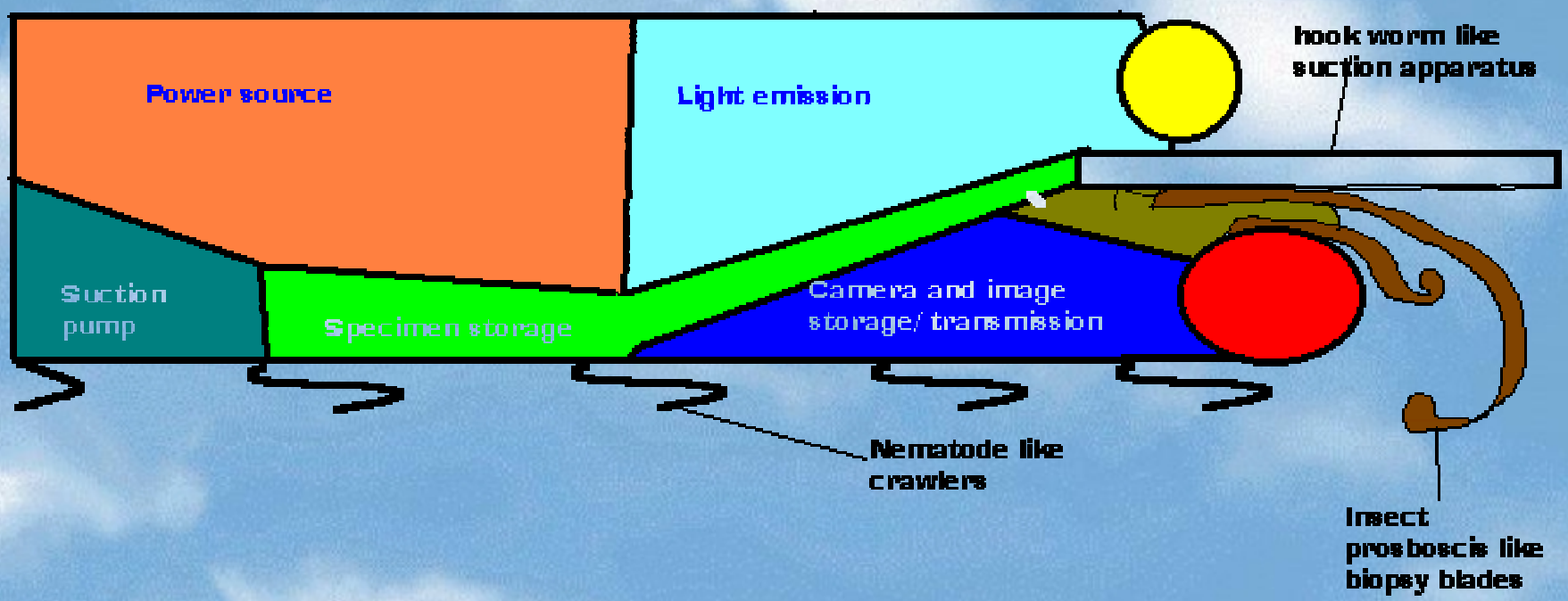
- Feasible design: Crawlers or floating apparatus designed after flukes and millipedes, Cytology brush, flexible forceps, aspiration needles, & retrievable baskets in conventional scopes replaced with cutting tools designed after human parasites & insects
- Patient discomfort can be avoided
- Adverse effects from endoscopy can be minimized as no vagal nerve stimulation, no anesthesia or sedation, less perforation risk
- Can bypass partial obstruction due to small size
- Multiple sites could be biopsied by numerous rovers
- Lowered cost
- Minimize cross contamination

Bio-inspiration from insects and human parasites

Bio-inspired Oncologic diagnostic prototype



Bio-inspired Oncologic diagnostic prototype

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