Domain Knowledge related to Thesis

What Are Cells and Their Role?

A **cell** is the **basic building block of life**. Every tissue and organ in your body is made of cells.

Key Functions of Cells:

Function	Description
Growth & Repair	Cells divide to help you grow and replace damaged tissues.
Energy Production	Cells convert food into energy to fuel body processes.
Defense	Some cells (like white blood cells) fight infections and diseases.
Communication	Cells send signals to coordinate actions in tissues and organs.
Reproduction	Cells divide to produce new cells; reproductive cells make babies.

Special Note in Cancer:

- In **malignancies**, cells **lose normal control**.
- They divide uncontrollably, don't die when they should, and can **invade tissues or travel through lymph or blood** to spread cancer.

What is a Malignancy?

A **malignancy** is another word for **cancer**. It refers to a group of cells in the body that:

1. **Grow uncontrollably** – Unlike normal cells, malignant cells divide rapidly without the usual controls.
2. **Invade nearby tissues** – They can spread into surrounding healthy tissues.
3. **Can metastasize** – Malignant cells can travel through the blood or lymph system to other parts of the body and form new tumors.

Difference Between Benign and Malignant Tumors

Feature	Benign Tumor	Malignant Tumor (Malignancy)
Growth	Slow	Rapid
Spread	Stays in one place	Invades nearby tissue
Metastasis	No	Yes, can spread to distant organs
Risk	Usually low	Life-threatening if untreated
Example	Lipoma (fat tumor)	Oral squamous cell carcinoma

In Oral Cancer

- Malignant cells in the **oral cavity** are the ones that **form tumors**, invade surrounding tissues (like tongue, gums, cheeks), and can eventually spread to lymph nodes or other organs.
- The most common malignancy in the mouth is **Oral Squamous Cell Carcinoma (OSCC)**.

What is the Lymphatic System?

The **lymphatic system** is a part of your **immune and circulatory systems**. It is made up of:

- **Lymph** – A clear fluid that carries **white blood cells** and nutrients.
- **Lymph vessels** – Tubes that transport lymph throughout the body (like veins but for lymph).
- **Lymph nodes** – Small bean-shaped structures that **filter harmful substances** and help fight infections.
- **Other organs** – Spleen, tonsils, and thymus are also part of the lymphatic system.

Role:

- **Fights infections:** Lymph nodes trap bacteria, viruses, and abnormal cells (like cancer cells).
- **Transports fluids:** Returns excess fluid from tissues back to the blood.
- **Helps in cancer spread:** Malignant cells can travel through lymph vessels to other parts of the body (this is called **metastasis**).

Visual analogy: Think of it like a **highway system** for immune cells, carrying "soldiers" (white blood cells) to fight invaders and sometimes accidentally carrying cancer cells to new places.

Definition:
Oral cancer encompasses malignancies in the mouth and surrounding areas, including the lips, tongue, cheeks, gums, and palate. The most prevalent form is **Oral Squamous Cell Carcinoma (OSCC)**.

Risk Factors:

- **Tobacco use** (smoking and smokeless)
- **Alcohol consumption**
- **Human Papillomavirus (HPV) infection**
- **Poor oral hygiene**
- **Sun exposure** (lip cancer)

Symptoms:

- Persistent mouth ulcers
- Unexplained lumps or thickening
- Difficulty swallowing or chewing
- White or red patches in the mouth

1. How Oral Cancer Spreads

Oral cancer mainly spreads in two ways:

a) Local invasion

- Cancer grows into nearby tissues in the mouth:
  - Tongue → floor of mouth
  - Gums → jawbone
  - Lips → cheek

b) Metastasis (Distant spread)

- Cancer cells can travel through:
  - **Lymphatic system** → lymph nodes in the neck
  - **Bloodstream** → distant organs

Common organs affected by metastasis from oral cancer:

- **Lymph nodes in neck** (most common)
- **Lungs**
- **Liver**
- **Bones**

2. Symptoms Indicating Spread to Other Organs

Organ	Possible Symptoms from Oral Cancer Spread
Lymph nodes (neck)	Swollen lumps, painless or tender, hard or fixed
Lungs	Persistent cough, shortness of breath, chest pain
Liver	Abdominal pain, jaundice (yellow skin/eyes), fatigue
Bones	Bone pain, fractures, limited movement in jaw or other bones

Important: These symptoms do **not appear in all patients**, but when present, they indicate advanced disease and require further diagnostic tests.

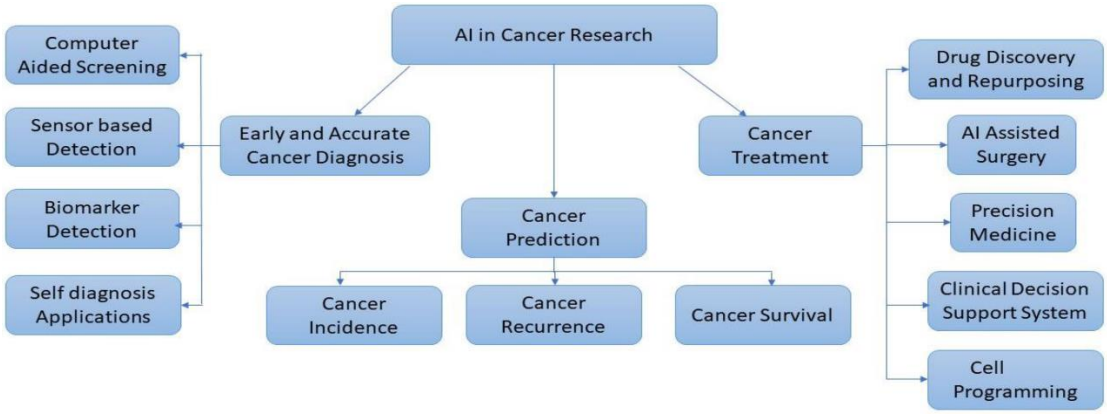
Global and National Landscape

- **Global Incidence:**
  Oral cancer is among the top 10 most prevalent cancers worldwide, with significant cases in Southeast Asia.
- **Pakistan's Scenario:**
  In Pakistan, oral cancer ranks as the second most common cancer among men, particularly prevalent in regions like Punjab and Sindh. Early detection remains a challenge due to limited screening programs.

AI in Oral Cancer Research

Artificial Intelligence (AI) has shown promise in enhancing early detection, diagnosis, and treatment planning for oral cancer. Here's how:

- **Early Detection:**
  AI algorithms, especially deep learning models, analyze clinical images to identify early signs of oral cancer, often outperforming traditional methods.
- **Histopathological Analysis:**
  AI assists in examining tissue samples, aiding in accurate diagnosis and prognosis.
- **Risk Assessment:**
  Machine learning models predict the likelihood of malignancy based on various patient data.



Modalities Use for Oral cancer:

1. Clinical Examination (Primary Screening)

- **Visual Inspection:** Dentists or doctors look for white or red patches, ulcers, or unusual lumps in the mouth.
- **Palpation:** Feeling the tongue, lips, and gums to detect abnormal masses.
- **Toluidine Blue Staining:** A dye that highlights abnormal oral mucosa areas.

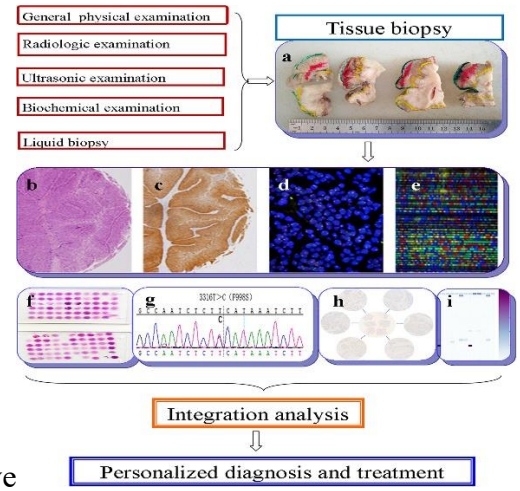
Pros: Simple, inexpensive, non-invasive.
Cons: Can miss early-stage lesions; requires experienced clinicians.

2. Imaging Modalities

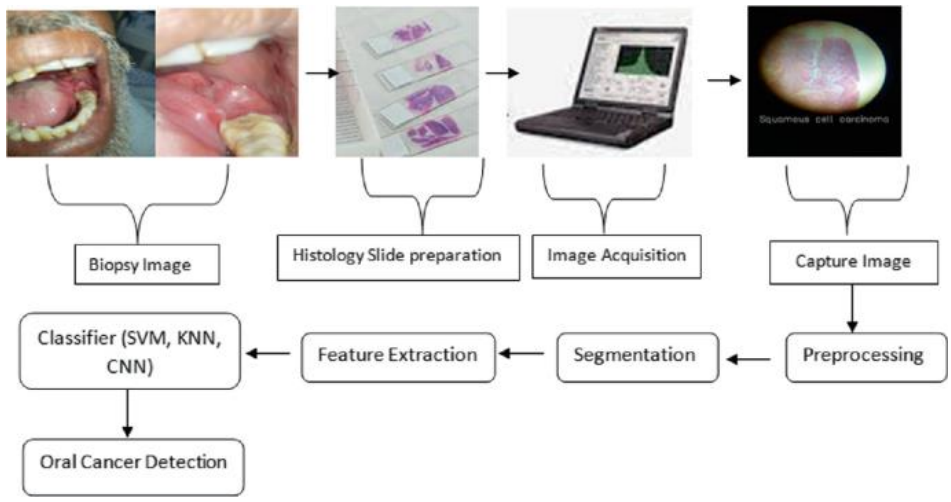
Modality	Purpose	Notes
CT Scan (Computed Tomography)	Detect tumor size, depth, and invasion of nearby tissues	Good for bone involvement
MRI (Magnetic Resonance Imaging)	Visualize soft tissue involvement and tumor boundaries	High contrast for soft tissue
PET Scan (Positron Emission Tomography)	Detect metastasis (spread) to lymph nodes or distant organs	Often combined with CT (PET/CT)
Ultrasound	Examine cervical lymph nodes for metastasis	Safe, real-time, low cost

3. Cytology (Less Invasive)

- **Brush Biopsy / Exfoliative Cytology:** Cells are scraped from the lesion and examined under a microscope.



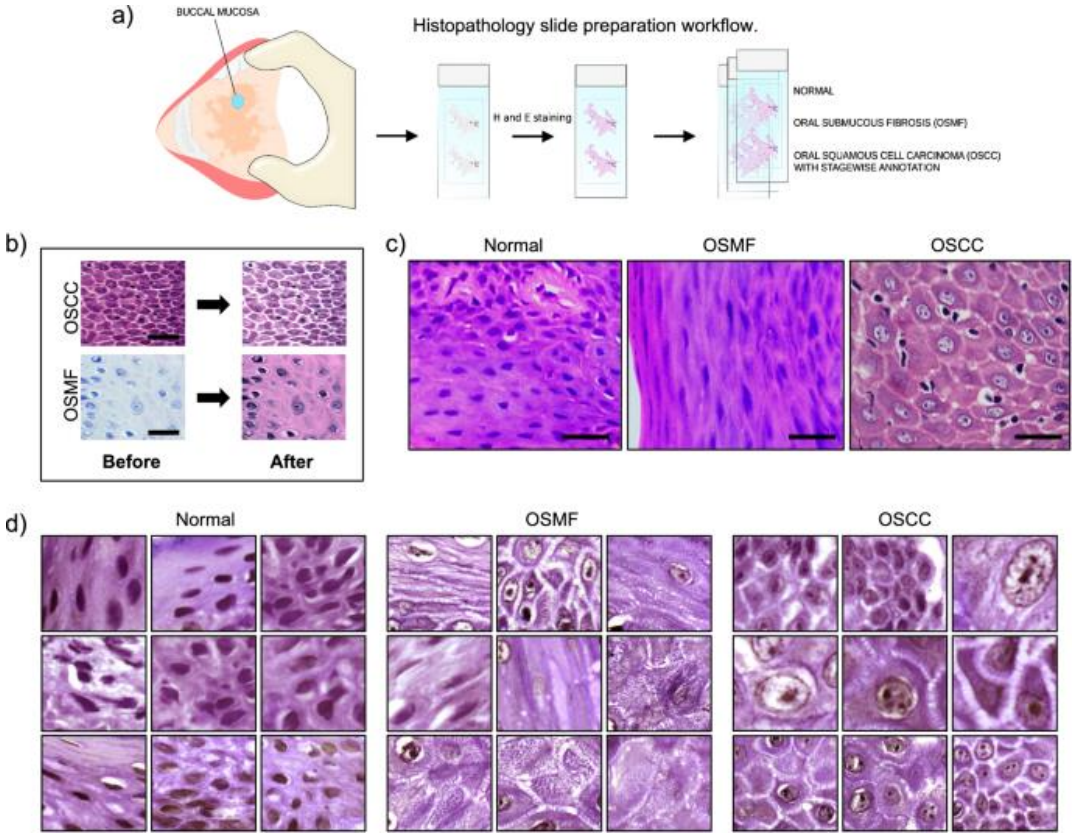
- **Use:** Good for screening; not always definitive



4. Histopathology (Gold Standard)

- **Biopsy:** Small tissue sample is taken from the suspicious lesion.
- **Examination under microscope:** Pathologist checks for **malignant cells** (like oral squamous cell carcinoma).

Pros: Definitive diagnosis.
Cons: Invasive, requires lab processing.

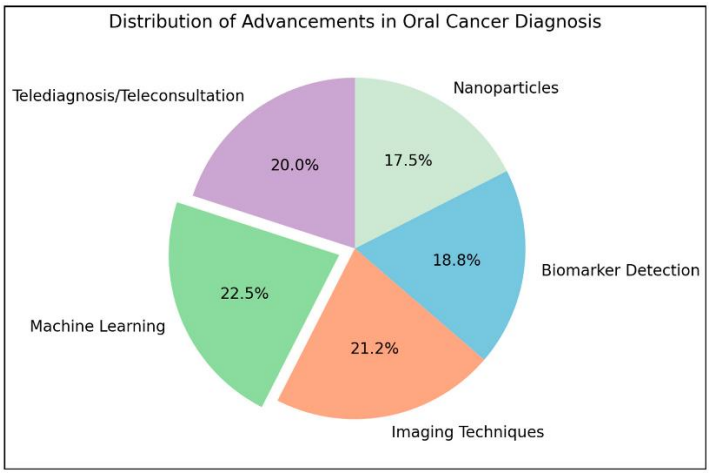


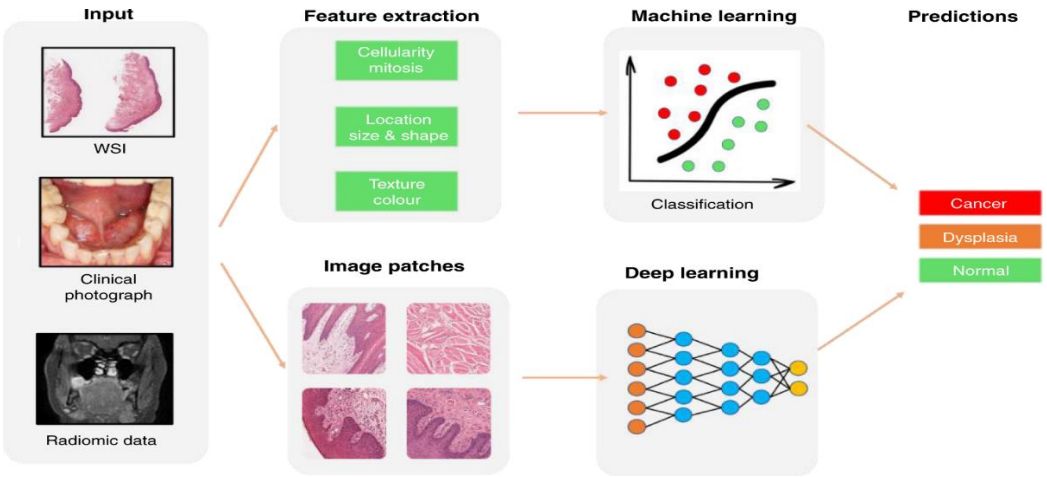
5. Molecular / Biomarker Tests

- **Saliva-based Tests:** Detect genetic mutations or protein markers linked to oral cancer.
- **Blood Tests:** Identify circulating tumor DNA (ctDNA) or other biomarkers.
- **Use:** Research and early detection.

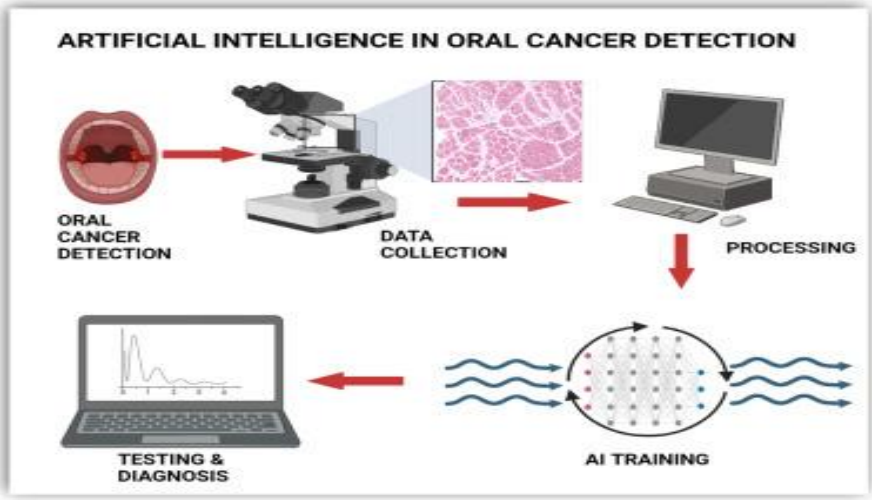
6. AI and Digital Modalities (Emerging)

- **Image Classification:** Using AI to detect oral lesions in photographs.
- **Histopathology AI:** Deep learning models to classify tissue slides automatically.
- **Multi-modal AI:** Combines images, biomarkers, and patient data for risk prediction.
- **Pros:** Non-invasive, fast, can assist clinicians in early detection.
  Cons: Needs datasets, validation, and regulatory approval.





Detailed AI based Modalities in Oral Cancer Diagnosis:



1. Deep Learning for Image Analysis

- **Application**: Utilizes convolutional neural networks (CNNs) to analyze clinical, radiological, and histopathological images for early detection and classification of oral squamous cell carcinoma (OSCC).
- **Example**: A study developed a multimodal deep learning framework integrating DenseNet-121 CNNs, achieving high accuracy in detecting OSCC from clinical, radiological, and histopathological images. arXiv

2. Machine Learning for Prognostic Modeling

- **Application**: Employs machine learning algorithms like support vector machines (SVM), k-nearest neighbors (KNN), and neural networks to predict patient outcomes, survival rates, and treatment responses.
- **Example**: Research indicates that integrating feature selection and dimensionality reduction techniques with machine learning models can enhance the prediction accuracy for oral cancer prognosis. arXiv

3. AI-Driven Biomarker Discovery

- **Application**: Combines multi-omics data (genomic, transcriptomic, proteomic) with AI to identify potential biomarkers for early oral cancer detection.
- **Example**: A study leveraged AI models to integrate multi-omics data, identifying biomarkers that could enhance the clinical detection of oral cancer. ScienceDirect

4. Speech Signal Analysis

- **Application**: Analyzes vocal characteristics using machine learning to detect throat cancer, which can be related to oral cancer.
- **Example**: A scoping literature review highlighted the potential of machine learning in detecting throat cancer from speech signals, though it noted the lack of open science and standardized methodologies in this area. arXiv

Identified Research Gaps in AI for Oral Cancer

1. Data Heterogeneity and Limited Datasets

- **Challenge**: Variability in data sources, image quality, and patient demographics hampers the generalization of AI models.
- **Impact**: Limits the applicability of AI tools across diverse populations and clinical settings.

2. Integration of Multi-Modal Data

- **Challenge**: Combining clinical, radiological, and histopathological data into cohesive AI models remains complex.
- **Impact**: Potential loss of valuable information and reduced diagnostic accuracy.

3. Lack of Standardization and Validation

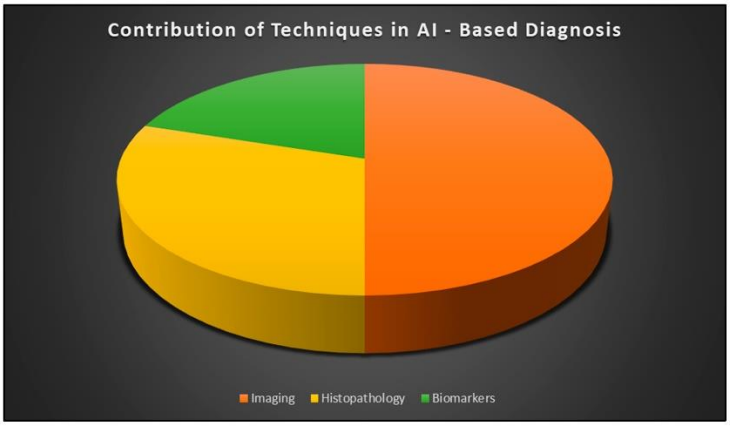
- **Challenge**: Absence of standardized protocols for AI model development and evaluation.
- **Impact**: Inconsistent performance and difficulty in clinical adoption.

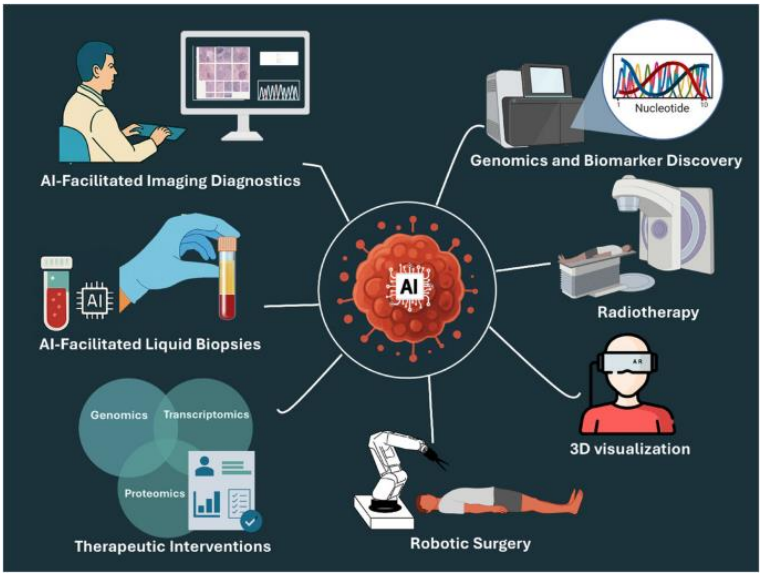
4. Ethical and Regulatory Concerns

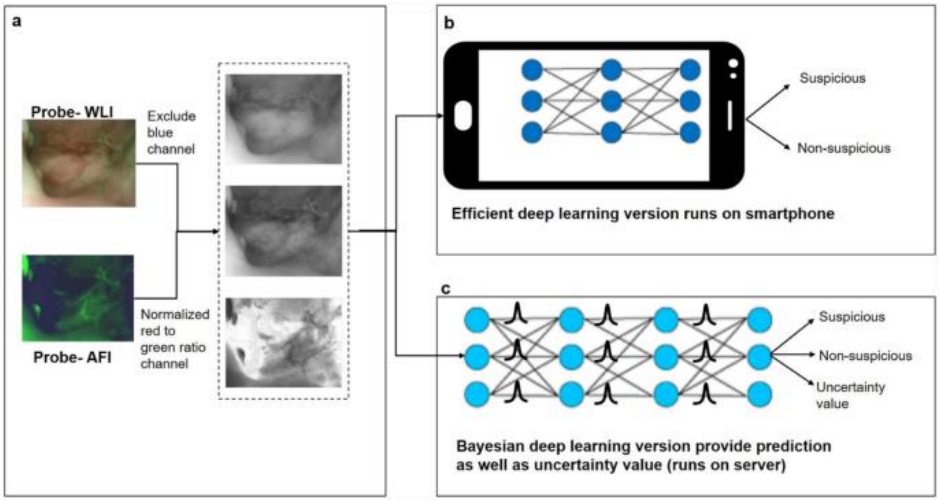
- **Challenge**: Issues related to data privacy, informed consent, and AI decision-making transparency.
- **Impact**: Ethical dilemmas and potential resistance from healthcare providers and patients.

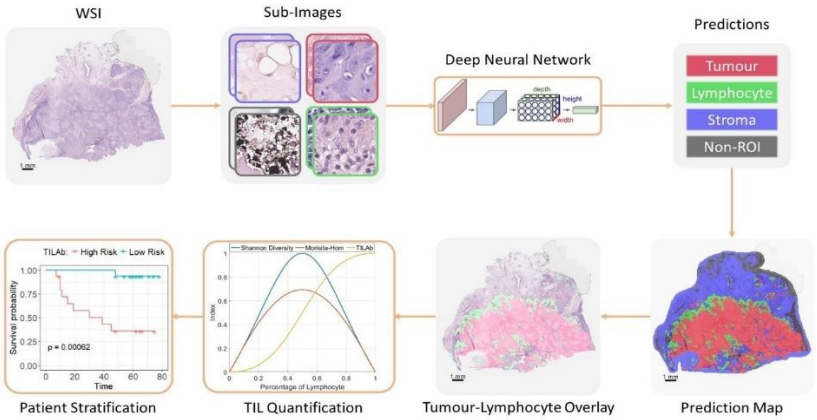
5. Real-World Implementation Barriers

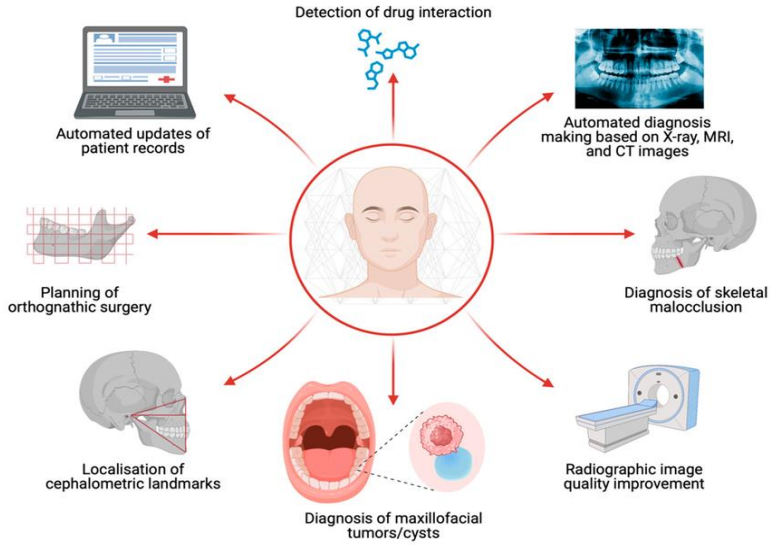
- **Challenge**: Limited integration of AI tools into routine clinical practice.
- **Impact**: Delayed adoption and underutilization of AI advancements in oral cancer care.

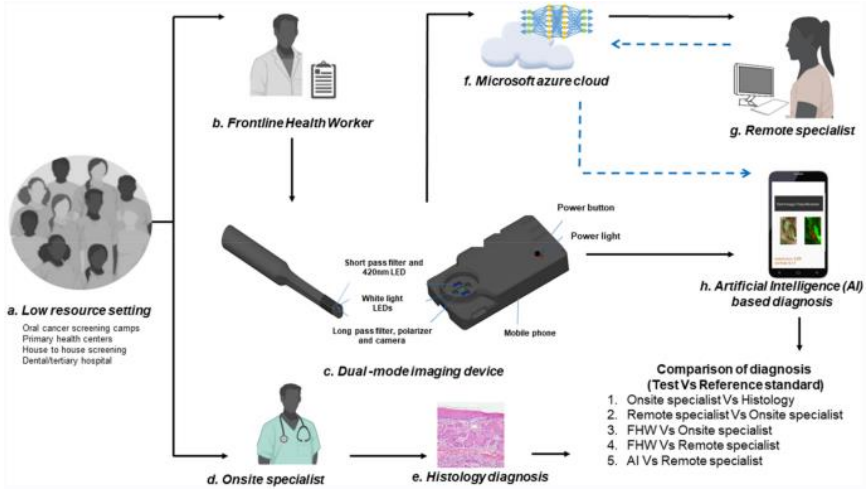

Contribution of Techniques in AI - Based Diagnosis
Imaging
Histopathology
Biomarkers

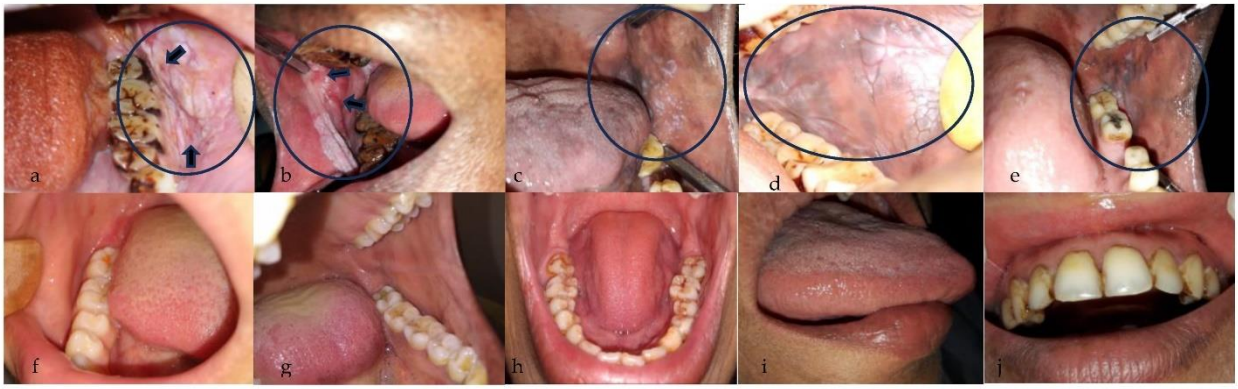

AI-Facilitated Imaging Diagnostics
Genomics and Biomarker Discovery
Nucleotide
AI
AI-Facilitated Liquid Biopsies
Radiotherapy
Genomics
Transcriptomics
Proteomics
Therapeutic Interventions
3D visualization
Robotic Surgery


a
Probe- WLI
Exclude blue channel
Probe- AFI
Normalized red to green ratio channel
b
Suspicious
Non-suspicious
Efficient deep learning version runs on smartphone
c
Suspicious
Non-suspicious
Uncertainty value
Bayesian deep learning version provide prediction as well as uncertainty value (runs on server)

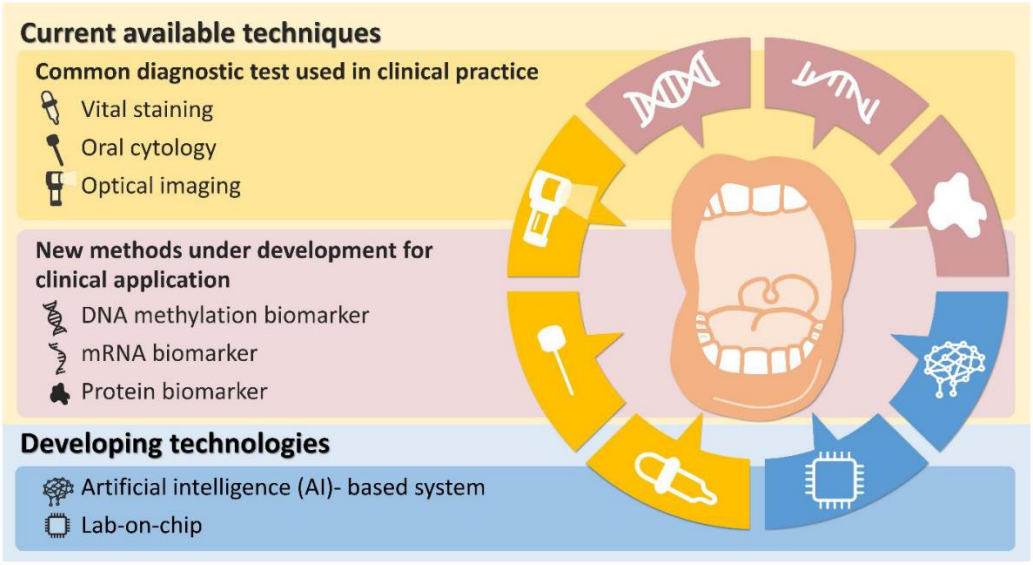

WSI
Sub-Images
Deep Neural Network
Predictions
Tumour
Lymphocyte
Stroma
Non-ROI
TILAb: High Risk Low Risk
Survival probability
p = 0.00062
Time
Shannon Diversity Morisita-Horn TILAb
Index
Percentage of Lymphocyte
Patient Stratification
TIL Quantification
Tumour-Lymphocyte Overlay
Prediction Map


Detection of drug interaction
Automated updates of patient records
Automated diagnosis making based on X-ray, MRI, and CT images
Planning of orthognathic surgery
Diagnosis of skeletal malocclusion
Localisation of cephalometric landmarks
Radiographic image quality improvement
Diagnosis of maxillofacial tumors/cysts


a. Low resource setting
Oral cancer screening camps
Primary health centers
House to house screening
Dental/tertiary hospital
b. Frontline Health Worker
f. Microsoft azure cloud
g. Remote specialist
Power button
Power light
Short pass filter and 420nm LED
White light LEDs
Long pass filter, polarizer and camera
Mobile phone
c. Dual-mode imaging device
h. Artificial Intelligence (AI) based diagnosis
d. Onsite specialist
e. Histology diagnosis
Comparison of diagnosis
(Test Vs Reference standard)
1. Onsite specialist Vs Histology
2. Remote specialist Vs Onsite specialist
3. FHW Vs Onsite specialist
4. FHW Vs Remote specialist
5. AI Vs Remote specialist



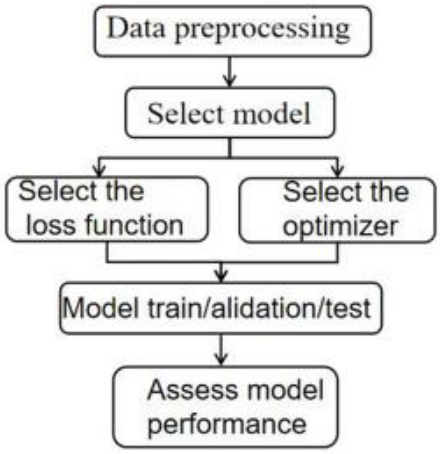
In nut shell:

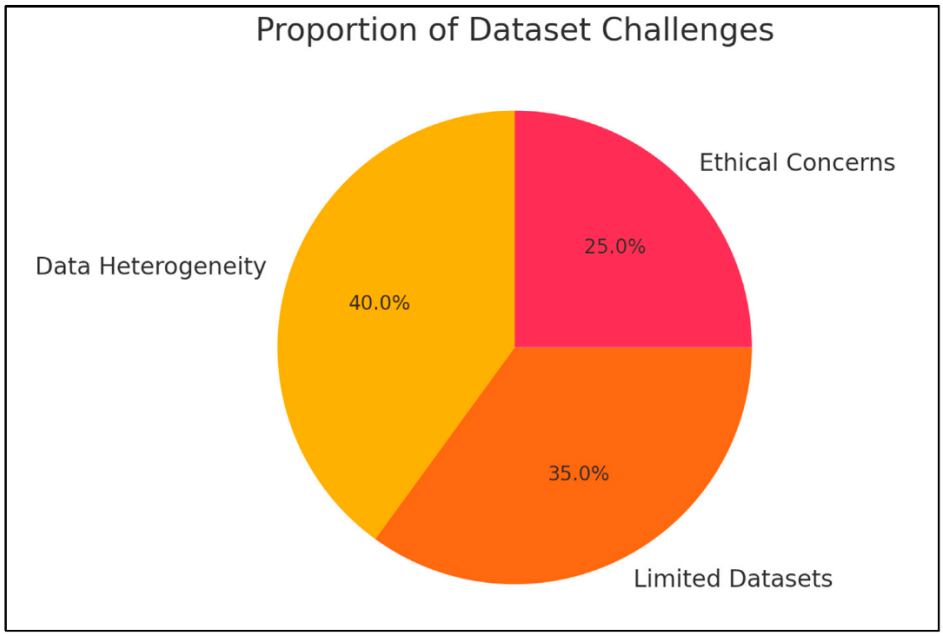


Acquisition Tools

Data Collection

Deep Learning Model





What is Multi-Modality AI in Oral Cancer Diagnosis?

Multi-modality AI means combining **different types of data** to improve diagnosis or prognosis. For oral cancer, possible modalities include:

Modality Type	Examples
Clinical Images	Photos of lesions, white/red patches, ulcers
Histopathology Images	Microscopic slides of biopsied tissue
Radiology Images	CT scans, MRI, PET scans
Molecular / Genomic Data	Gene expression, saliva biomarkers, mutation data
Patient Data	Age, gender, tobacco/alcohol use, lifestyle

Goal: AI learns from **all these sources together** rather than separately, producing more accurate predictions.

Why Multi-Modality is Powerful

- Some cancers **look similar visually**, but histology or genetic data reveals differences.
- Some early signs might **not appear in images**, but molecular markers detect disease.
- Combining modalities allows AI to **catch subtle patterns** that single-modality approaches miss.

What is Prognosis?

Prognosis is a **medical term** that describes the **likely outcome or course of a disease** for a patient. It tells doctors and patients **what to expect in the future**, including:

- **How the disease may progress** (get better, stay the same, or worsen)
- **Chances of recovery or survival**
- **Likelihood of recurrence** (disease coming back)
- **Expected complications**

In the Context of Cancer

For cancer patients, **prognosis** often involves predicting:

- **Survival rates** – e.g., 5-year survival for oral cancer patients.
- **Response to treatment** – which therapies are most likely to work.
- **Risk of metastasis** – chance that cancer will spread to lymph nodes or other organs.
- **Recurrence probability** – likelihood of cancer returning after treatment.

Factors Affecting Prognosis in Oral Cancer:

Example

- A patient with **small, early-stage oral cancer** that hasn't spread has a **good prognosis** – high chance of cure.
- A patient with **advanced oral cancer that has spread to lymph nodes** has a **poor prognosis** – lower survival rate and higher risk of recurrence.

Factor	Effect on Prognosis
Stage of cancer	Early-stage cancers have better outcomes
Tumor size	Smaller tumors are easier to treat
Lymph node involvement	Spread to lymph nodes worsens prognosis
Patient health	Overall health and comorbidities impact survival
Treatment type	Surgery, radiotherapy, chemotherapy, or combination
Genetic/biomarker profile	Some mutations can worsen or improve outcomes

Recent Review Papers on Oral Cancer and AI

To deepen your understanding, consider exploring the following recent review articles:

1. **"Insights Into AI-Enabled Early Diagnosis of Oral Cancer"**
   Published in 2025
   This paper discusses the potential of AI in enhancing early diagnosis, particularly in low-resource settings. It highlights various AI techniques and their applications in oral cancer detection.
   Read the full article here
2. **"Assessing Artificial Intelligence in Oral Cancer Diagnosis"**
   Published in 2025
   This study reviews twelve papers demonstrating AI applications in diagnosing oral cancer, focusing on lesion identification and prognostic prediction using machine learning and deep learning algorithms.
   Access the study on PubMed
3. **"Revisiting Early Detection of Oral Cancer: A Review on Methods, Impact on Survival Rates, and Recurrence Prevention"**
   Published in 2025
   This review emphasizes the importance of early detection in improving survival rates and preventing recurrence, discussing various diagnostic methods and their effectiveness.
   Read the article here

Exploring these publicly available datasets:

1. **Oral Cancer Dataset (Kaggle):**
   A collection of clinical images and patient data useful for training AI models in oral cancer detection.
2. **ISBI Oral Lesion Dataset:**
   Provides histopathological images for studying tissue-level changes in oral lesions.
3. **Shaukat Khanum Cancer Registry:**
   Offers clinical and demographic data specific to Pakistan, aiding in region-specific research.

Novel Idea for Research

Here's an idea that could be **new and research-worthy**:

AI Model Concept

- **Inputs:**
    1. Oral lesion images (from clinical exams)
    2. Histopathology slides (microscopic images)
    3. Saliva-based biomarker levels or genomic data
    4. Patient demographic & lifestyle data
- **Process:**
    - Use a **multi-branch neural network**, where each branch processes one modality:
        - CNN branch for lesion images
        - CNN / Vision Transformer branch for histopathology images
        - Dense network branch for genomic/biomarker data
        - Another dense branch for patient demographics
    - **Fuse features** from all branches using concatenation or attention mechanisms
    - Final layer predicts:
        - Likelihood of malignancy
        - Stage of oral cancer
        - Risk of metastasis
- **Output:**
  AI provides **a probability score** for cancer detection and severity, improving early diagnosis.

Research Gap / Novelty

Most existing studies focus on **one or two modalities**:

- Clinical images only
- Histopathology only
- Radiology only

Novelty:

- No widely implemented **AI model combines clinical images + histopathology + saliva biomarkers + patient history** for oral cancer diagnosis.
- Could be first to develop a **truly multi-modal AI model** for **early detection + metastasis prediction**.

Steps to Implement Your Research

1. **Data Collection:**
    - Clinical oral lesion images (photos)
    - Histopathology slides from biopsy datasets
    - Saliva/genomic data from research studies
    - Patient demographics from registries like **Shaukat Khanum**
2. **Preprocessing:**
    - Normalize images, extract features from biomarker/genomic data
    - Encode categorical patient info
3. **Model Design:**
    - Multi-branch neural network (CNN + Dense layers + Attention)
    - Train on labeled datasets (malignant vs benign, stage info)
4. **Validation & Testing:**
    - Compare multi-modal AI performance vs single-modality models
    - Use metrics like **accuracy, AUC, sensitivity, specificity**
5. **Expected Outcome:**
    - Early detection with higher accuracy
    - Prediction of metastasis risk
    - Integrates all available data into a single tool

Tip for Novel Research:

- Focus on **low-resource settings** like Pakistan where oral cancer is common
- AI could help **screen large populations** using multi-modal data
- Add explainable AI (XAI) to show **which modality contributes most** to diagnosis