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Review Article

Biopsy: The benchmark for diagnostic excellence amidst advanced technological advancements – A review

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ABSTRACT

Biopsy remains a critical diagnostic tool for identifying oral lesions, vital for establishing a definitive diagnosis through the examination of both physical and microscopic tissue abnormalities. Despite technological advancements, biopsy is still the most trusted method among oral healthcare professionals, particularly when clinical, radiographic, and histopathological findings do not align. However, challenges can arise, such as inadequate tissue sampling or the need for deeper analysis. This article explores the skills and potential pitfalls in biopsy procedures, emphasizing the importance of integrating clinical and radiological information to uphold biopsy as the gold standard in diagnosis, even in today's advanced technological landscape.

1. Introduction

In 1966, the World Health Organization (WHO) defined biopsy as "The examination of tissue removed from a lesion." The term "biopsy" has its origin from two Greek words, where "bios" means life and "opsis" means vision, indicating a minor surgical procedure to extract tissue from a living organism.[1] Biopsy serves two primary purposes: establishing a definitive diagnosis to guide treatment and assessing prognosis by confirming whether the affected tissue has been completely removed with clear margins. Histopathological diagnosis, traditionally the most precise, solidifies biopsy's status as the gold standard among diagnostic and investigative procedures.[1,2]

Although advanced imaging and investigative techniques have lessened the need for biopsies in some areas, biopsy remains essential for diagnosing mucosal lesions in the oral cavity. In dentistry, it's common for practitioners to treat oral lesions without a biopsy, and excised tissue is not always sent for histopathological examination.[3] However, it is crucial that all tissue removed from oral lesions undergo histologic evaluation.[4]

This paper discusses the key aspects of biopsy procedures for oral lesions, covering indications, contraindications, biopsy types, procedural guidelines, potential errors, and diagnostic challenges. It aims to equip general dentists with insights to enhance patient treatment options.

Oral lesions are common, and biopsy decisions depend on the situation. Some require immediate biopsy, others after follow-up, while some may not be biopsied due to potential complications associated with the underlying conditions. This paper aims to guide oral health professionals on when biopsy is indicated or contraindicated to prevent complications.[5,6] These indications and contra – indications are as follows:

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1.1. Indications

1. When an ulcer or growth persisting for more than 2 weeks, without any identifiable cause.
2. Any lesion suspected to be of inflammatory origin but is unresponsive to treatment even after 2 weeks.
3. Red or white lesion clinically suspected as potentially malignant
4. Any lesion suspected to be a cyst or neoplasm
5. Oral lesions of controversial etiology, especially when they are associated with pain or paresthesia
6. Patients having cancer phobia
7. Chronic reactive or inflammatory lesions like gingival growths
8. Lesions that interfere with mastication or speech like tori or fibrous hyperplasia
9. Recurrent mucosal lesions or suspicious changes in pre-existing lesions
10. Material from a persistent intraoral or extraoral draining sinus the source of which cannot be identified.
11. Any tissue surgically excised

1.2. Contra-indications

1. Systemically ill and debilitated patient
2. Presence of acute viral or bacterial infection
3. Hypermelanotic lesion suspected to be malignant melanoma (Only excisional biopsy done
4. Vascular lesions where hemostasis may be a problem
5. Parotid salivary gland neoplasm (only excisional biopsy done

2. Awareness on Types of Biopsy and Procedural Intricacies

The subsequent crucial aspect for an oral health professional is gaining an understanding of the various biopsy techniques and procedures. Oral biopsies can be categorized based on the technique employed, the tools used, the type of tissue sampled, and the timing of the biopsy. A simplified overview of the procedures involved in oral biopsies to assist in the oral health professional's comprehension of this vital aspect are as follows:

2.1. Technique used: [7–9]

1. Incisional biopsy: when only a particular representative part of a lesion is removed. [Figure 1A]
2. Excisional biopsy: when the entire lesion and a small margin of normal tissue is removed. It is the ideal treatment for small lesions (<1cm) [Figure 1B].
3. Imprint/ Touch biopsy: also known as touch preparation or scrape cytology, is a diagnostic technique used to assess lymph nodes for the presence of abnormal cells, particularly in cases where lymph node involvement is suspected due to infection or cancer.
4. Curettage biopsy: also known simply as "curettage" is a medical procedure that involves scraping or cleaning out body cavities for various purposes, including tissue sampling for diagnostic or therapeutic reasons.
5. Tru –cut needle biopsy: is a medical procedure used to obtain a core of tissue sample of about 2 mm in thickness from bony lesions for the diagnosis and assessment of bone abnormalities, including bone tumors, cysts, or other bone-related conditions.

2.2. Armamentarium or material used: [10–15]

1. Brush biopsy: also known as a 'transepithelial brush biopsy' or simply "brush biopsy," is a non-invasive diagnostic method used to detect cell atypia, particularly in potentially malignant disorders in the oral cavity. This technique involves gently brushing the surface of the oral mucosa or lesion with a special brush-like instrument designed to capture superficial epithelial cells. These collected cells are then examined under a microscope to assess for any signs of cell atypia or abnormal changes. [Figure 1C]
2. FNAB (Fine Needle Aspiration Biopsy): is a diagnostic procedure commonly used for a variety of purposes, including the evaluation of intra-osseous cysts, tumors, and salivary gland lesions. [Figure 1D]
3. Exfoliative cytology: also known as 'oral cytology', is a diagnostic technique that involves the microscopic examination of shed or desquamated epithelial cells from the surface of mucous membranes, particularly in the oral cavity. This method is commonly used for the detection of various oral conditions, including oral dysplasia.
4. Punch Biopsy: A punch biopsy is a medical procedure in which a small, cylindrical piece or "chunk" of tissue is removed from a suspected lesion or abnormal area for diagnostic purposes, to determine the nature of the lesion, whether it's benign, precancerous, or malignant. [Figure 1E]
5. Forceps: This instrument developed by Bermejo, histopathological [14]
6. Electrocautery: This approach offers the advantage of maintaining a bloodless field during the biopsy procedure because it cauterizes (seals) blood vessels, which can help improve visibility and reduce bleeding. However, it is important to be aware that there is also a potential risk of thermal damage associated with cauterization.
7. LASER: A soft tissue LASER scalpel, commonly CO2 LASER is used for and there is a lack of hemorrhage during the procedure. [Figure 1F]

2.3. Type of lesional tissue:[1]

1. Direct biopsy: is performed when the lesion is readily visible on the oral mucosa and can be easily accessed with a scalpel or other surgical instruments directly from the mucosal surface.
2. Indirect biopsy: is conducted when the lesion is not directly visible on the oral mucosa's surface and is instead covered by what appears to be normal-looking mucosal tissue. In this case, the clinician takes a tissue sample from the seemingly healthy mucosa surrounding the lesion

2.4. Time of the biopsy:[16]

1. Pre - operative biopsy: are conducted before surgery and are aimed at diagnosing a lesion or condition that requires surgical intervention.
2. Intra-operative biopsy: are performed during surgery itself. Surgeons may perform an intra-operative biopsy to confirm the nature of a lesion, ensure clear margins, or guide the extent of the surgical resection.
3. Post – operative biopsy: are conducted after surgery, typically as a follow-up procedure. These biopsies are aimed at checking the efficiency of the treatment and guide further management or adjustments as needed.

2.5. Miscellaneous[17–22]

1. Ultrasound guided needle biopsies: also known as 'ultrasound-guided percutaneous needle biopsies', are a medical procedure that combines the use of ultrasound imaging with a fine needle to obtain tissue samples from specific areas of the body (soft tissues and organs).
2. Stereotactic core biopsies: are a specialized medical procedure used primarily in the field of radiology to obtain tissue samples from suspicious or abnormal areas, particularly in the breast.
3. Endoscopic biopsies: also known as endoscopic mucosal biopsies or endoscopic tissue sampling, are medical procedures performed using an endoscope to obtain tissue samples from the interior of various body cavities, such as the gastrointestinal (GI) tract, respiratory system, and urinary tract**.**
4. Bone marrow biopsies: is a medical procedure used to obtain a sample of bone marrow tissue for diagnostic purposes. It is primarily performed to evaluate and diagnose various blood disorders, such as aplastic anemia, leukemia, myelodysplastic syndromes, and certain immune system disorders.

3. Preliminaries of the Biopsy Procedure

Before performing a biopsy procedure, there are several important preliminaries and preparatory steps that need to be taken to ensure the safety and effectiveness of the procedure. These preliminary steps may vary depending on the type of biopsy, the location of the lesion, and the patient's overall health.[23]Table 1 summarizes some of the common preliminaries for a biopsy procedure.

4. Disinfection of the Biopsy Site & Administration of Local Anesthesia

Disinfection and local anesthesia are crucial steps before a biopsy. The biopsy site should be disinfected with a non-iodinated antiseptic to avoid staining, and a local anesthetic like lidocaine should be used to numb the area, ensuring patient comfort and a sterile environment. These measures are essential for minimizing infection risk and procedural discomfort.[24]

4.1. The biopsy procedure

The biopsy procedure is a medical technique for obtaining tissue samples for diagnostic, investigative, or therapeutic purposes. The specific steps vary based on the biopsy type and tissue location.[4,25] Instruments and materials used can include standard surgical tools like scalpels, tissue forceps, and scissors, as well as specialized equipment such as punches, B-forceps, electrocautery, and lasers [Figure 1G]. Figure 2 gives a general overview of the common steps involved in a biopsy procedure.

The steps and techniques of a biopsy can vary based on the clinical context, tissue location, and biopsy type. The primary goal is to obtain a representative and diagnostic tissue sample while minimizing patient discomfort and reducing the risk of complications.

4.2. Biopsy artefacts

Biopsy artifacts can significantly impact the accuracy of histopathologic diagnosis. These artefacts may occur at various stages of the biopsy process, from the initial collection of the tissue sample to its processing and examination in the pathology laboratory.[26,27]Table 2 presents a comprehensive list of various artefacts that can occur during oral biopsy procedures, potentially affecting the accuracy of histopathological diagnoses.

4.3. The biopsy performa

When a biopsy is sent to the oral pathologist for histopathological analysis, a biopsy form is used. This form should include the reason for the biopsy and details such as the site, size, shape, color, texture, consistency, clinical presentation, associated signs or symptoms, lymph node status, and any systemic diseases [Figure 3]**.** The provisional or differential diagnosis should also be recorded. Sometimes, a diagram showing anatomical sites may be included, and surgical margins should be marked with

Table 1: Preliminaries for a biopsy procedure

Preliminaries	Description
Patient Evaluation	Evaluation of the patient's medical history, including any underlying health conditions, allergies, medications, and previous surgeries or procedures.
Informed consent	The healthcare provider discusses the purpose, risks, benefits, and alternatives of the biopsy procedure with the patient.
Anesthesia	The type of anesthesia to be used (local, regional, or general) is determined based on the biopsy location and the patient's comfort and safety.
Imaging	Imaging studies such as X-rays, CT scans, ultrasound, or MRI may be conducted before the biopsy to precisely locate the lesion or target area and guide the procedure.
Biopsy site markings	The biopsy site may be marked or identified using imaging guidance, skin markers, or other methods to ensure accurate targeting.
Monitoring	The patient's vital signs, such as heart rate, blood pressure, and oxygen saturation, may be monitored throughout the procedure, especially if anesthesia is administered.
Post – biopsy care	Post-biopsy care instructions and potential complications are discussed with the patient.

Table 2: Common artefacts during oral biopsy procedures

Artefacts	Description	Prevention
1. **Anoxia or Agonal changes**	• Due to delay in fixation resulting in mitochondrial damage • Nuclear pyknosis, karyolyis and karyorrhexis with cytoplasmic vacuolation	Tissue should be stored by 40^0 C or by rapid fixation
2. **Split artefact**	Occurs when the tissue sample is not properly handled or prepared, and it appears to be split or divided when viewed under a microscope.	Handle biopsy specimens carefully and follow proper tissue processing and sectioning protocols.
3. **Crush artefact**	Occurs due to improper pressure while handling the tissue using forceps, scissors or scalpel resulting in cell distortion, nuclear streaking and cellular degeneration.	It is essential to handle tissue specimens with care and precision, including the use of appropriate instruments and gentle handling.
4. **Compression artefact**	Due to minimal compression of the tissue, tissues can become distorted, displaying irregular serrated edges with cells that appear crushed and dark chromatin strands within their nuclei.	Handle the specimen carefully
5. **Curling artefact**	• more common in incisional biopsy • Due to the small size of the oral biopsy specimens, the tissue is not oriented properly during embedding procedure	Position the specimen with its mucosal surface facing upwards on a sterile piece of paper and ensuring adequate depth of specimen is achieved in biopsy specimens
6. **Foreign body artefact**	• Cotton fibers resemble fungal hyphae or appear as eosinophilic, resembling amyloid-like or black substances that exhibit polarization when viewed under polarized light. • Starch granules are characterized by their refractive properties, polygonal shape, positive staining with PAS (Periodic Acid-Schiff) stain, and a size range of 5 to 20 millimeters in diameter. They bear a resemblance to atypical epithelial cells.	Using rubber gloves alternately and accurately identifying foreign materials in biopsy specimens.
7. **Fulgeration artefact**	• When electrocautery is used, tissue protein coagulation may occur due to the heat generated and results in an amorphous appearance of the tissues. • With the use of LASER and electrocautery, the epithelial cells appear detached with a spindled, palisading configuration of the nuclei, separation of the epithelium from the basement membrane and amorphous opaque appearance of the muscle, fat and fibrous connective tissue	To prevent this issue, it's advisable to maintain a gap between the incisional margin and the boundary of the lesion and utilize a cutting electrode when collecting the specimen.
8. **Forceps artefact**	Occurs when the tooth forceps penetrates the specimen resulting in tears or voids along with compression of the stroma	• Avoid tooth forceps • Use B forceps • Proper care when taking the specimen

silk sutures to aid in specimen orientation and margin identification. We have designed a flowchart that may serve as a pathway for oral health professionals to follow in order to obtain an accurate biopsy sample [Figure 4].[28,29]

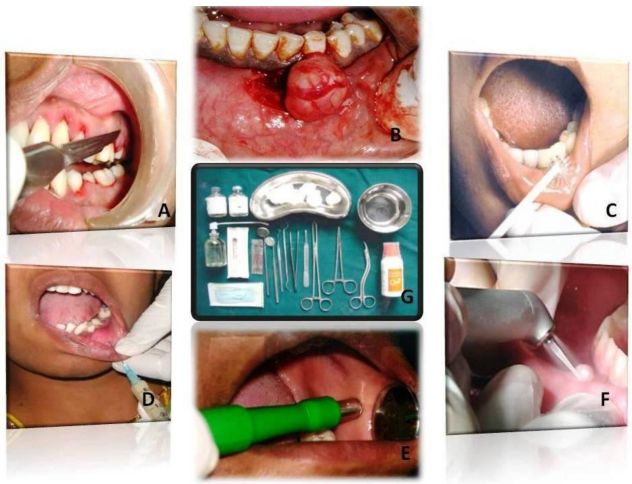

Figure 1: Various oral biopsy's procedures; **A** – Incisional biopsy, **B** – Excisional biopsy, **C** – Brush biopsy, **D** - Fine Needle Aspiration Biopsy, **E** – Punch biopsy, **F** – Laser, **G** - instruments and materials needed for performing a biopsy procedure

Figure 2: Overview of biopsy procedure

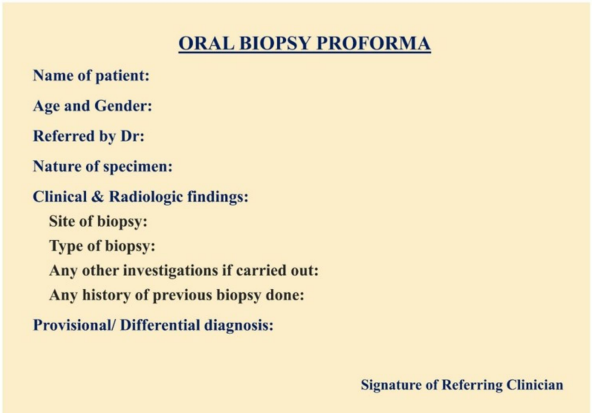

Figure 3: Oral Biopsy Proforma

Figure 4: Simple overview of the pathway to obtain biopsy sample

5. Complications Following Biopsy

As a dental practitioner and oral health practitioner, it is essential to be aware of potential complications from biopsy procedures and to discuss these with the patient beforehand. Common complications include postoperative bleeding, infections, nerve damage leading to paresthesia or anesthesia, pain, swelling at the biopsy site, and damage to adjacent structures or tissues. Thorough documentation and patient discussion are crucial for effective management and informed consent.[30]

Open and transparent communication with patients about potential complications, along with obtaining informed consent, is crucial before performing oral biopsies.

Dentists and oral health professionals should also have a comprehensive plan to manage and mitigate these complications if they arise. This proactive approach ensures patient safety and effective post-biopsy care.[31]

5.1. The histopathologic diagnosis

There are 3 ways in which the pathologist may report the diagnostic biopsy:[1]

1. Definitive diagnosis: When distinctive features of a disease, such as squamous cell carcinoma with well-defined margins, tissue infiltration, invasion depth, and comprehensive histological grading, are observed, a definitive diagnosis can be made.
2. Incompatibility diagnosis: When essential diagnostic criteria are missing and clinical correlation is lacking, it is crucial to investigate potential sampling or processing errors.
3. Orientative diagnosis: When a pathologist cannot reach a definitive diagnosis, they may describe the observed histopathological features. It is important to emphasize that these findings should be clinically correlated or further investigated to support a conclusive diagnosis.

6. Conclusion

Oral biopsies are commonly conducted diagnostic procedures, particularly for various oral lesions, including potentially malignant disorders and oral cancer. However, despite their apparent simplicity, these procedures require careful planning and expertise to yield valuable diagnostic insights. Achieving a successful biopsy involves several key considerations, such as accurate site selection, precise incision depth within the tissue, and proper handling and processing of the collected tissue. Crucially, the effectiveness of this diagnostic procedure as the gold standard hinges on the collaborative efforts of a multidisciplinary team, including the oral physician, oral radiologist, oral surgeon, and oral pathologist. Their coordinated work ensures that patients receive the most accurate and comprehensive assessment, facilitating appropriate treatment and care.

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None.

8. Conflict of Interest

None.

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