



Labial minor salivary gland biopsy

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KEYWORDS

Lip biopsy;
 Minor salivary gland;
 Sjogren's syndrome;
 Xerostomia;
 Labial biopsy

Biopsy of the labial minor salivary glands ("lip biopsy") is often used as part of the diagnostic workup for suspected Sjogren's syndrome, and is comparable in diagnostic accuracy to open parotid biopsy. While there are non-invasive tests that should be performed for Sjogren's workup, in challenging cases tissue diagnosis provides valuable information. When properly performed, this office procedure can be done with minimal discomfort for the patient. The indications, risks, and interpretation of lip biopsy are discussed along with a detailed description of a technique designed to ensure sufficient tissue for diagnosis.

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Biopsy of the labial minor salivary glands ("lip biopsy") as a means of diagnosing Sjogren's syndrome was first popularized by Chisholm and Mason in 1968.¹ Before their landmark publication, few authors discussed minor salivary biopsy, and incisional biopsy of the major salivary glands was the intuitive choice for diagnosis of a disease that often manifested with parotid swelling. Parotid biopsy risked sialoceles and salivary fistula formation, injury to the facial nerve, and guaranteed an external incision, making alternative approaches attractive. Atkin and colleagues described an intraoral approach of parotid biopsy based on Seward's technique of salivary calculi removal,² therefore avoiding the external incision and risk of cutaneous fistula.³ However, this technique requires deep dissection through the buccinator and buccal fat, and still places the facial nerve at risk.

Biopsy of labial minor salivary glands avoids these risks and is technically straightforward to perform. Studies comparing lip biopsy to parotid biopsy have found these two techniques generally comparable in diagnosing Sjogren's.^{4,5} One study comparing 77 patients with simultaneous biopsies of the parotid and labial salivary glands⁶ found more abnormalities present in the parotid biopsies, but the meaning of these abnormalities is questionable in the setting of diagnosing Sjogren's syndrome because the study did not use currently accepted diagnostic criteria. A more recent study of 35 patients comparing simultaneous biopsies⁴ us-

ing the current United States-European Union diagnostic criteria (including standardized pathologic interpretation) found the same sensitivity (78%) and specificity (86%) with both procedures.

One of the technique's greatest pitfalls is that many operators fail to obtain sufficient minor salivary gland tissue in the sample to make the pathologic diagnosis. Even though it is called a "lip biopsy," the diagnosis does not require mucosa, but rather several lobules of the glandular tissue underneath.

Lower lip numbness has consistently been reported as the only long-term complication of lip biopsy, occurring in 0% to 6% of patients.⁴⁻¹⁰ Despite this established complication, which in our and others' experience is typically transient and of little distress to the patient, we still prefer labial minor salivary gland biopsy over parotid biopsy as our initial procedure, given the avoidance of external scar and the small but potentially catastrophic risk of facial nerve injury. We will perform biopsy of the tail of the parotid gland in patients who have nondiagnostic minor salivary biopsies and continued need for tissue diagnosis.

Indications

A patient is typically referred by a rheumatologist or neurologist as part of a work-up for suspected Sjogren's syndrome. This disease is common and estimated to affect between 0.4 and 3.1 million adults in the United States alone.¹¹ However, the majority of the patients have the

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classic Sjogren's manifestations of dry eyes and dry mouth and positive serologies (Ro/SS-A, La/SS-B, Rheumatoid Factor, or Antinuclear Antibody) and are diagnosed without tissue confirmation. Patients with atypical manifestations in whom the clinical picture is less clear tend to require tissue diagnosis. Rarely, inpatients with severe manifestations, such as paraplegia, might even be the subject of an inpatient consultation for lip biopsy. Many patients referred for the procedure do not fit the classic description of Sjogren's syndrome, and in these cases, a request for tissue from a competent referee is probably sufficient justification for the procedure.

Patients who have recently been on corticosteroids,¹² or who smoke,¹³ may have altered or uninterpretable results. Radiation to the oral cavity destroys salivary tissue and interferes with the usefulness of salivary gland biopsy.

Operative procedure

The patient's lower lip is inspected for a suitable incision site. The lower lip affords the best exposure for the operation, but the palate and buccal mucosa are potential alternative sites, if needed.¹ The incision should be placed away from mucosal abnormalities and hardware associated with dental appliances and should be below the bite line to avoid interference with the stitches. Patients can be queried regarding on which side of their mouth they chew and the contralateral side used if there are no other contraindications.

A small wheal of local anesthetic with a vasoconstrictor is raised in the mucosa. A chalazion clamp (Figure 1) is placed on the lower lip with the excision site in the middle of the oval. The clamp is then secured firmly, and the compression provides additional hemostasis, retraction of the lip, and pouthing of the mucosa. Using a fine blade, a 5- to 10-mm horizontal elliptical incision is made just through the mucosa and the ellipse is removed using toothed forceps. The salivary tissue should be visible (Figure 2). The cutaneous nerves supplying sensation (terminal branches of V3) to the lower lip are usually found between the mucosa

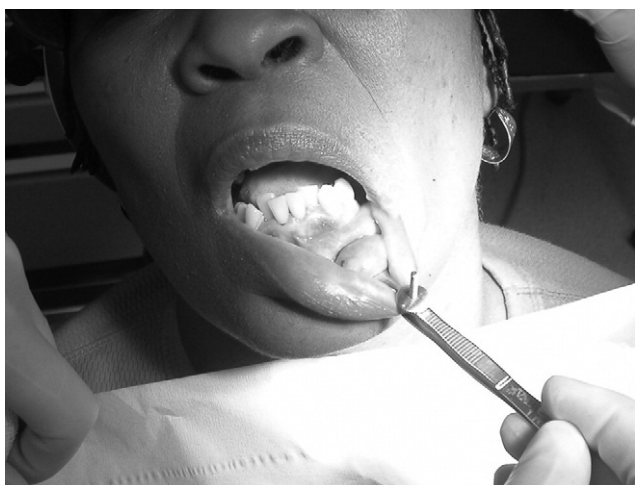


Figure 1 A chalazion clamp is secured on the lower lip to provide hemostasis and retraction.



Figure 2 An elliptical lower lip incision is made with a no. 15 blade and the mucosa removed to reveal the salivary tissue underneath.

and muscle, somewhat intertwined with the salivary tissue. Using sharp dissecting scissors, the submucosal tissue is spread in a vertical direction (parallel to the nerves) to further expose the minor salivary glands (Figure 3) and remove them. Care is taken to preserve the nerves. The salivary tissue is grasped using forceps and collected in a formalin transport container. It is very important to obtain enough tissue for diagnosis, defined roughly as three to seven lobules of glandular tissue. Any bleeding can be addressed with needle tip cautery, and then the mucosa is reapproximated using absorbable sutures (Figure 4).

Patients are given pain medicine and chlorhexidine mouthwash to use three times a day after meals for 10 days.

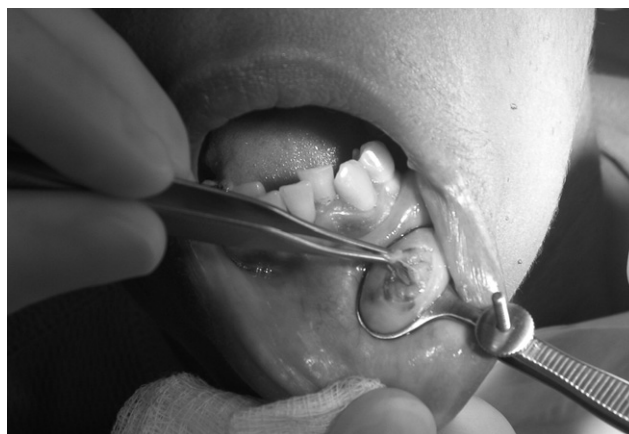


Figure 3 Salivary lobules are teased out of the lip, with care to preserve the sensory branches of V3.

Patients are counseled to avoid spicy or acidic foods for 1 week while the mucosa heals. Follow-up by phone should occur in 1 week to assess for complications.

Complications

Complications include bleeding, bruising, wound infection, pain, and numbness.

As discussed, the most common long-term complication is paresthesia of the lower lip. In addition, it must be remembered that saliva has important lubricating and antimicrobial properties; when lacking, patients are at increased risk for complications from oral surgery. Nonhealing wounds and infected mucosa can conceivably occur. We have found that the use of chlorhexidine mouthwash and avoidance of any irritating dental appliance use during the healing period can prevent these complications. When consenting patients, it is also important to mention the possibility of bleeding and retained suture material.

Discussion

Currently, biopsy of the minor salivary gland is included in several sets of diagnostic criteria, including the most commonly cited United States–European Union criteria.¹⁴ Other major criteria include ocular and oral dryness symptoms, a positive Schirmer's test or rose bengal score, positive salivary sialography, or scintigraphy, and the presence of autoantibodies.

Patients should be counseled that, even in the setting of sufficient tissue, nondiagnostic results can occur. False positives and negatives are also common in many series, although much of this may be due to pathologic technique.^{9,10} Histologically, it is the presence of focal sialadenitis that makes the diagnosis of Sjogren's syndrome.^{1,15} Focal sialadenitis is defined as an aggregate of 50 or more lymphocytes within the salivary gland tissue.¹ The grading system established by Chisholm and Mason¹ has been revisited by several authors; the most successful modification

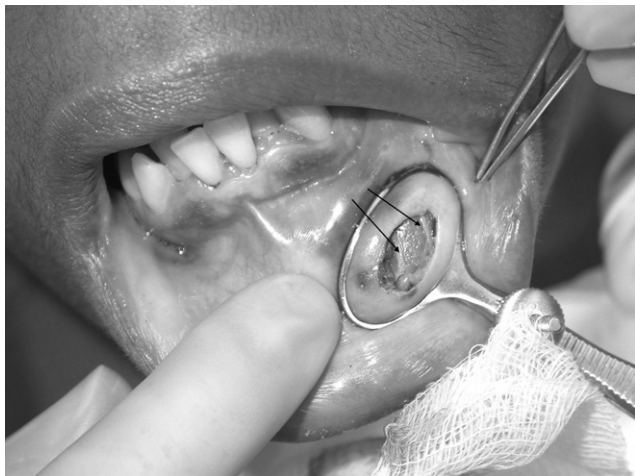


Figure 4 After removal of the salivary tissue, hemostasis is achieved and the mucosa reapproximated with absorbable suture. The arrows indicate the sensory branches of V3.

Table 1 The Currently Accepted "Focus Score" Pathologic Grading System for the Diagnosis of Sjogren's syndrome¹⁶

Focus Score	No. of Lymphocytic Foci per 4 mm ²
0	None or a small aggregate or infiltrate
1	One aggregate of 50 or more lymphocytes
2-11	Two to eleven aggregates (raw number)
12	Twelve aggregates or confluent infiltrate

A focus is defined as an aggregate of 50 or more lymphocytes per 4 mm². Depending on the Sjogren's diagnostic criteria that is being used, a focus score cutoff of either "1" or "greater than 1" is considered positive for Sjogren's syndrome.

being that of Greenspahn and colleagues,¹⁶ who developed the modern minor salivary gland "focus score" grading system (Table 1).

As more is learned about the immunology of Sjogren's syndrome and more sensitive techniques are developed for interpretation of salivary tissue samples and serologic markers, the need for tissue diagnosis may decrease or even be obviated by other, less invasive tests. For now, lip biopsy remains one of the mainstays of the work-up for Sjogren's syndrome.

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