

# Comparative Study of Frozen and Paraffin-Embedded Sections: Evaluation of Inflammatory Dermatoses

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**ABSTRACT:** **Background:** Frozen section (FS) is often performed when histopathological evaluations are urgently required for implementation of therapeutic measures. In dermatology, this method is most commonly used to evaluate excision margins of tumors. FS are also routinely employed to differentiate toxic epidermal necrolysis from staphylococcal scalded skin syndrome. However, little is currently known about the performance of FS in the diagnosis of inflammatory dermatoses.

**Objectives:** To compare histopathological diagnoses in a series of patients with a clinical diagnosis of an inflammatory dermatosis for which FS and paraffin-section (PS) specimens were obtained on the same day.

**Methods:** We conducted a single-center retrospective analysis of 43 cases. All histological slides were reviewed by a single dermatopathologist. Concordance was calculated between FS and PS.

**Results:** Patients were divided into three groups according to diagnosis: papulosquamous diseases (group I), drug eruptions (group II), and a heterogeneous group (group III) that included cases of bullous vasculitis and Sweet syndrome. Among the three groups, the results of FS and of PS were discordant only in five cases (5/43, 11.6%). Compared to PS, FS had a sensitivity of 92.9% [95% confidence interval (95%CI) 64.17–99.63%] and specificity of 100% in group I, sensitivity of 90.9% (95%CI 57.12–99.52%) and specificity of 100% in group II, and sensitivity of 83.33% (95%CI 60.78–94.16%) and specificity of 100% in group III. The degree of agreement between the results of the FS and of the PS was almost perfect (kappa = 0.95, 0.93 and 0.85 respectively).

**Conclusions:** This study suggests that FS is a valid approach for the rapid diagnosis of inflammatory dermatoses. This method is as specific as PS, although it is less sensitive.

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**KEY WORDS:** frozen section (FS), paraffin section (PS), inflammatory dermatosis

in a large percentage of surgical cases [1]. FS is now routinely used in many medical settings [2]. The literature stresses the necessity and importance of this technique in the operating room setting and in dermatology daily practice, mainly for evaluating metastatic disease and determining surgical borders during minimally invasive procedures [3–7].

FS procedure entails a few fundamental steps: freezing, fixation, cutting, and eventually dying with hematoxylin-eosin stain (H&E) [8]. In dermatology, the use of FS is at the core of Mohs' surgery for diagnoses as varied as non-melanoma skin cancer (NMSC) [9], dermatofibrosarcoma protuberans [10], microcystic adnexal carcinoma [11], extramammary Paget's disease [12], and lentigo maligna [13]. FS is also routinely used for the diagnosis of non-malignant conditions including erythema multiforme, Stevens–Johnson syndrome, toxic epidermal necrolysis [14], and staphylococcal scalded skin syndrome [15]. To the best of our knowledge, frozen sections are not regularly implemented in the context of the diagnosis of inflammatory skin dermatosis. However, although not a common practice, in our department FS are sometimes used for this purpose, subject to clinical considerations. In this article we review the accuracy of this method for this process.

## PATIENTS AND METHODS

The files of all patients admitted to the Department of Dermatology at Sourasky Tel Aviv Medical Center during the years 2010–2014 were reviewed. Included were patients with clinical suspicion of inflammatory dermatosis for whom both FS and paraffin-section (PS) specimens were obtained. No exclusion criteria were defined. Both biopsies were taken at the same time, from the same lesion. FS slides were examined on the same day they were taken, and PS histopathological results were provided 3–7 days later by the same dermatopathologist since there is only one trained dermatopathologist in our medical center. For relevant patients we retrospectively compared FS results to the pathological diagnosis, regarded as the “gold standard,” to assess concordance. The study was performed according to the ethics committee approval.

The frozen section (FS) procedure was first described by Louis B. Wilson. In his work published in 1905, he concluded that a diagnosis can be made from an FS preparation

**STATISTICAL ANALYSIS**

Sensitivity and specificity were evaluated in the following manner: discrimination ability was evaluated using the area-under-the-receiver operating characteristic (ROC) curve. Cohen’s kappa coefficient was used to measure the agreement between the new test, FS, and the gold standard, PS. Threshold values proposed by Landis and Koch for interpretation of the Kappa coefficient were used.

**RESULTS**

A total of 43 patients fulfilled the inclusion criteria and were included in the study. To evaluate FS parameters in different clinical scenarios, cases were divided into three major categories according to their final diagnoses: papulosquamous diseases (n=14), drug eruptions (n=11), and others (n=18).

Since erythema multiforme is most commonly induced by an infection rather than by drugs [16,17], such cases were classified as group III. Any discrepancies between PS and FS were also documented. We ascertained the performance of the FS approach as compared with delayed examination of PS using the statistical model described above [Table 1]. FS was characterized by a sensitivity of 92.9% and specificity of 100% for the diagnosis of papulosquamous diseases [Figure 1], a sensitivity of 90.9% and a specificity of 100% for the diagnosis of drug eruptions [Figure 2], and a sensitivity of 83.33% and specificity of 100% for other diagnoses [Figure 3]. The degree of agreement between the results of the FS and PS was almost perfect (kappa = 0.95, 0.93 and 0.85 respectively).

**DISCUSSION**

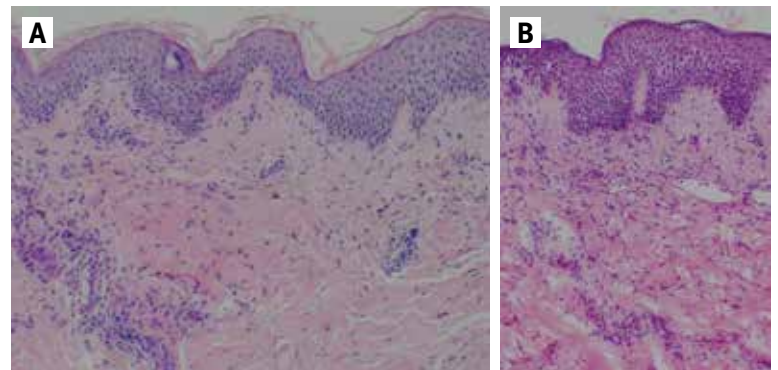
Accurate diagnosis is often critical when choosing an effective and safe treatment. However, a clinical diagnosis of skin diseases may be challenging as the clinical information and appearance of cutaneous lesions may overlap. Histopathological examination of skin biopsies plays a pivotal role in the dermatological diagnostic process [18].

Processing of PS is both labor and time consuming as it requires tissue fixation, grossing, processing, embedding, and staining [19]. In situations in which a definitive diagnosis needs to be reached rapidly, FS can be employed. Its role has been firmly established for the diagnosis of predominantly malignant diseases but, as demonstrated here, it can be useful in the diagnosis of inflammatory dermatoses as well. For example, erythroderma is among the most common manifestations of inflammatory skin disorders requiring a rapid diagnosis to initiate an effective treatment. In our study group, three patients (3/43) with erythroderma were eventually diagnosed with psoriasis (n=2) or a psoriasiform drug eruption (n=1), leading to administration of cyclosporine or cessation of the offending drug, respectively. Similarly, FS was

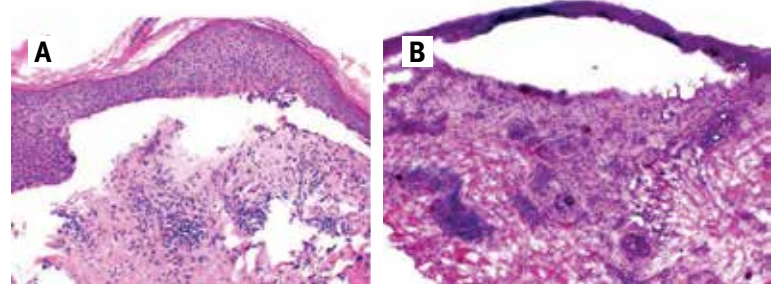
**Table 1.** Sensitivity and specificity of frozen section method in the different groups (n=43)

|             | Papulosquamous diseases (n=14) | Drug eruptions (n=11) | Heterogeneous group (n=18) |
|-------------|--------------------------------|-----------------------|----------------------------|
| Sensitivity | 92.9%                          | 90.9%                 | 83.33%                     |
| Specificity | 100%                           | 100%                  | 100%                       |

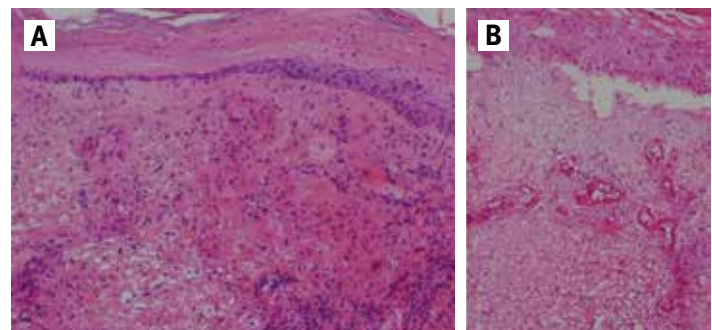
**Figure 1.** Histopathological findings in a patient with psoriasis. **[A]** Paraffin-embedded section and **[B]** frozen section (hematoxylin-eosin, original magnification ×40 and 100 respectively)



**Figure 2.** Histopathological findings in a patient with bullous dermatosis. **[A]** Paraffin-embedded section and **[B]** frozen section (hematoxylin-eosin, original magnification ×40 and 100 respectively)



**Figure 3.** Histopathological findings in a patient with cutaneous vasculitis. **[A]** Paraffin-embedded section and **[B]** frozen section (hematoxylin-eosin, original magnification ×100 and 200 respectively)



recently shown to aid in the diagnosis of a newborn with bullous congenital ichthyosiform erythroderma (epidermolytic hyperkeratosis) [20].

FS can also be helpful in the diagnosis of bullous dermatoses, by demarcating the level of bulla formation and differentiating the diagnosis from a rapidly progressing life-threatening drug eruption, with good sensitivity and specificity. In our study, differentiation of pemphigus vulgaris from pemphigus foliaceus was possible utilizing FS. Likewise, FS seems to be a very accurate modality in atypical clinical cases of Sweet syndrome and cutaneous vasculitis.

FS has no absolute contraindications; however, it has some limitations, mostly regarding sampling technique and the pathologist's experience [2,21]. These limitations can be overcome by sound experience and careful implementation of the technique.

Our study has a few limitations. Our sample size was relatively small with a total of 43 patients. All data were collected from a single hospital, which may lead to a certain selection bias of patients. This was a non-blinded study as both FS and PS evaluations were done by the same dermatopathologist. This bias is somewhat limited by a few factors. First, the pathologist was unaware of the study's existence and purpose since this was a retrospective study. Second, FS and PS evaluations were done several days apart due to the high volume of work in the pathology department in our institute, which may provide some validity to the pathologist's consistency. Further studies are needed to support or refute this hypothesis, preferably multicenter, double-blinded studies.

In conclusion, our data imply that FS can serve as a valuable tool in the diagnosis of various inflammatory dermatosis when a pathological diagnosis is rapidly required. Further studies are needed to confirm this hypothesis.

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#### “Expert: a man who makes three correct guesses consecutively”

Laurence J. Peter (1919–1990), Canadian educator and “hierarchologist” best known to the general public for the formulation of the Peter principle, namely, the concept in management whereby the selection of a candidate for a position is based on the candidate's performance in their current role, rather than on abilities relevant to the intended role. Thus, employees only stop being promoted once they can no longer perform effectively, and “managers rise to the level of their incompetence”