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None disclosed.

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The accuracy of detecting melanoma on frozen section melanoma antigen recognized by T cells 1 (MART-1) stains and on permanent sections of previously frozen tissue: A prospective cohort study

To the Editor: Mohs micrographic surgery (MMS) for melanoma is controversial because of concerns about the accuracy of detecting melanoma on frozen sections. This study's primary analysis examined the sensitivity and specificity of detecting melanoma using hematoxylin and eosin (H&E) and melanoma-associated antigen recognized by T cells (MART-1) frozen sections compared with permanent sections. The secondary analysis evaluated whether frozen section specimens can be subsequently processed for permanent sections without diminishing diagnostic accuracy.

This Institutional Review Board-approved prospective study enrolled consecutive consenting adults (aged >18 years) with biopsy-proven *in situ* or invasive melanoma treated with MMS with frozen section MART-1 immunohistochemical stains (MMS-IHC) from 2016 to 2018. All melanomas were excised with a previously published MMS-IHC protocol.[1]

Two opposing vertical sections were isolated from the melanoma debulking excision (Fig 1). One specimen (frozen-to-permanent) was processed for frozen sections, then thawed and processed for permanent sections. The opposing study specimen (direct-to-permanent) was immediately fixed in formalin for permanent sections. All frozen sections were stained with both H&E and MART-1 and were evaluated by a single Mohs micrographic surgeon. All permanent sections were stained with H&E, but MART-1 was ordered at the discretion of the dermatopathologist. Permanent sections were evaluated by 1 of 5 dermatopathologists, who were blinded to the interpretation of the Mohs micrographic surgeon and whether or not the specimen had been previously frozen.

Pathologic interpretations were categorized into 4 groups: (1) malignant; (2) benign; (3) qualified malignant; (4) qualified benign (see Supplemental Table I for definitions, available via Mendeley at https://data.mendeley.com/datasets/hrjjcr43nx/1). A positive result (melanoma detected) was defined as diagnosis of "malignant" or "qualified malignant." A negative result (melanoma not detected) was defined as diagnosis of "benign" or "qualified benign."

Tissue samples from 169 consecutive patients, comprising 119 melanoma *in situ* (70.4%) and 50 invasive melanomas (29.6%) were evaluated (Table I). The primary analysis showed that the Mohs micrographic surgeon detected melanoma on frozen sections (test specimen) with a sensitivity of 95.3% (95% confidence interval [CI], 89.6%-98.1%) and a specificity of 95.1% (95% CI, 82.2%-99.2%) compared with the dermatopathologist's permanent section interpretation of the same study specimen (frozen-to-permanent; gold standard) (Fig 1).

The secondary analysis showed that dermatopathologists detected melanoma on the frozen-to-permanent sections (test specimen) with a sensitivity of 98.3% (95% CI, 93.6%-99.7%) and a specificity of 89.6% (95% CI, 76.6%-96.1%),

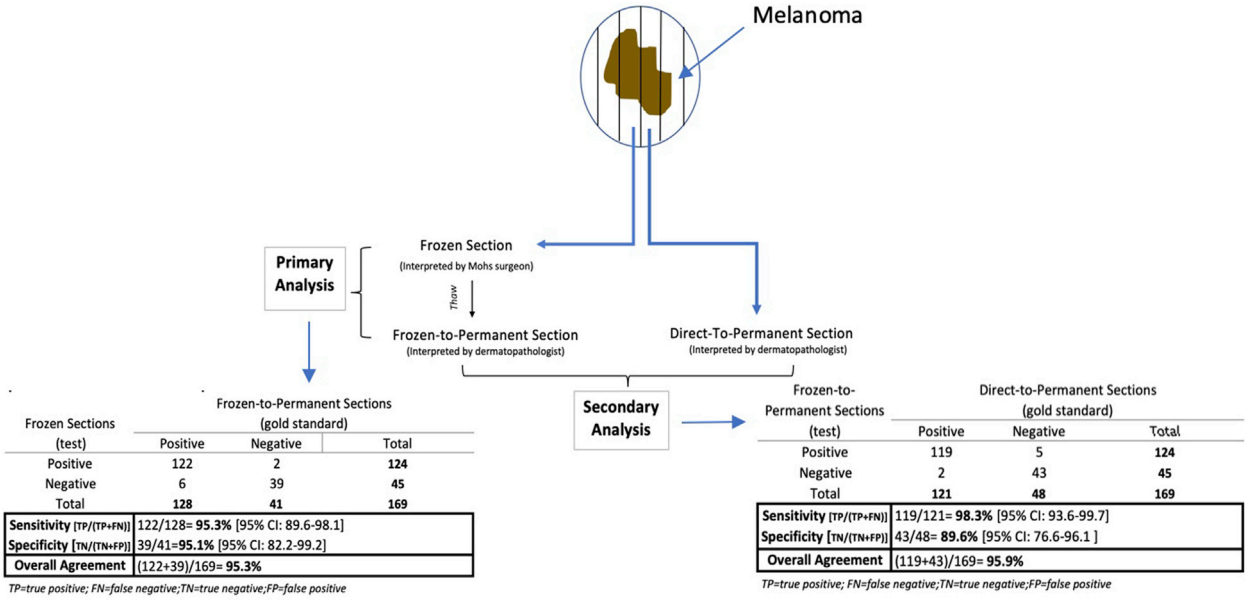

Fig 1. Tissue processing methodology. *CI*, Confidence interval; *FN*, false negative; *FP*, false positive; *TN*, true negative; *TP*, true positive.

Table I. Characteristics of the study cohort

Variable*	Number of Patients (%) (N = 169)
Sex	
Male	104 (62)
Female	65 (38)
Age, y	67.7 (37-101)
Preoperative diagnosis	
Melanoma *in situ*	119 (70)
Lentigo maligna type	65
Superficial spreading	1
Acral lentiginous	1
Not specified	52
Invasive melanoma	50 (30)
Lentigo maligna	30
Superficial spreading	14
Nodular	3
Not specified	3
Depth of invasion, mm	
<1	41
1-2	7
>2-4	1
Not specified	1
Anatomic location	
Head and neck	147 (87)
Hands or feet	5 (3)
Pretibial leg	4 (2.3)
Trunk or extremity (nonacral, non-pretibial)	13 (7.7)

*Data are presented as number of patients (%) or as mean (range).

compared with their own interpretation of the direct-to-permanent sections (gold standard) (Fig 1). Of the 15 total discordant diagnoses from both analyses, 12 involved specimens with a qualified diagnosis, indicating the challenge of diagnosing these specimens (Supplemental Fig 1).

This study shows that Mohs micrographic surgeons detect melanoma on H&E and MART-1 frozen sections with high accuracy compared with dermatopathologists' interpretation of permanent sections. It also shows that dermatopathologists detect melanoma on permanent sections of previously frozen tissue with high accuracy compared with specimens sent directly for permanent sections. Therefore, Mohs micrographic surgeons can thaw challenging frozen sections for second opinions with diagnostically accurate permanent sections. Diagnostic discordances are expected for challenging melanocytic tumors.[2-4]

Although this study is limited by its single-center design, it demonstrates that MMS-IHC is a reliable technique to detect melanoma. It supports the use of MMS-IHC for precise microscopic margin-directed excision of *in situ* and invasive melanoma.

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Conflicts of interest

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Risk factors for thick melanoma among veterans: A cross-sectional study

To the Editor: Breslow thickness is the most important melanoma prognostic factor, with mortality increasing by 1.6-fold for every millimeter increase.[1] Prior research suggests that dermatology visits at 6 months[2] and 24 months[3] before diagnosis are associated with thinner melanomas, but the optimal interval remains unknown. We examined risk factors for thick melanoma (≥2 mm) versus thin (<2 mm) at diagnosis, including timing of prior dermatology visits.

In this cross-sectional study, we retrospectively identified initial invasive melanoma diagnoses (1 per subject) documented in the VA Central Cancer Registry, capturing approximately 90% of VA cancer cases[4] from January 2009 to December 2017, when prevalence stabilized. We examined thickness and several covariates, including last dermatology visit (Table I). We examined typical screening skin examination intervals, including visits 6 or 12 months before diagnosis (±2 weeks). We also examined visits outside of these points that were within 2 years and 2 to 5 years of diagnosis. Cases with missing or inaccurate thickness based on tumor stage were excluded. We conducted univariate and multivariable logistic regression to determine odds of thick melanoma (≥2 mm), using R version 3.5.3. The VA Boston Healthcare System institutional review board approved this study.

We identified 19,504 melanoma cases. After excluding 7286 cases (37.4%) for missing thickness and 105 (0.5%) for incongruent thickness, 12,113 cases (62.1%) remained. Most patients were men and 94% were regular VA users,[5] with no difference between those with thin and thick melanomas. Veterans with thick melanoma were more likely to be older, be minority race/ethnicity, be North Atlantic/Pacific residents, have extratruncal locations, and be less likely to have dermatology visits less than or equal to 2 years after diagnosis compared with those with thin melanoma (Table I). On multivariable analysis, older age, Black race, Hispanic ethnicity, North Atlantic/Pacific residency, and extratruncal locations were associated with increased odds of thick melanoma (Table II). Dermatology visits 6 months (odds ratio [OR] 0.31; 95% confidence interval [CI] 0.24-0.39) or 12 months (OR 0.40; 95% CI 0.31-0.52) before diagnosis were associated with similarly reduced odds of thick melanoma. Dermatology visits at nonscreening intervals were