

## Resolving a differential diagnosis of metastatic malignant melanoma or malignant fibrous histiocytoma

*Monongalia General Hospital, Morgantown, WV*

**Provisional Diagnosis:** Monophasic synovial sarcoma or malignant fibrous histiocytoma

**Reference Laboratory Diagnosis:** Metastatic malignant melanoma

**Final Confirmed Diagnosis:** Malignant fibrous histiocytoma

### Initial Staining/Scan History:

- Immuno stain 1 (Monongalia): Positive for vimentin only with negative S100, cytokeratins, EMA, CD34, and desmin
- Immuno stain 2 (reference lab): Focally S100 and HMB-45 positive
- Immuno stain 3 (Monongalia): Vimentin positivity, focal EMA positivity in areas with epithelioid cell morphology and bluish S100 staining ambiguous for interpretation. HMB-45 again negative, as was wide-spectrum Cytokeratin, CK7, CK20, CD34, smActin, Desmin, Factor VIII, NSE, CD68, and CD138
- Immuno stain 4 (reference lab): S100 positivity in epithelioid areas, HMB45 negative, and Melan-A negative

### Case Summary:

A 44-year-old male patient presented at Monongalia General Hospital with a large (20cm), left posterior chest lesion. An initial biopsy evaluated by the hospital's pathology lab rendered a provisional diagnosis of soft tissue neoplasm with monophasic synovial sarcoma or malignant fibrous histiocytoma in the differential.

The case was sent for consultation to an academic reference laboratory. This group provided a diagnosis of malignant melanocytic tumor consistent with metastatic malignant melanoma.

Three months later, the patient underwent definitive therapy with wide excision and axillary lymph node dissection. Monongalia forwarded the case to the reference laboratory again, which ran additional immuno stains, and found 18 lymph nodes negative for malignancy. The reference laboratory confirmed a diagnosis of residual malignant melanocytic tumor most consistent with metastatic malignant melanoma.

But Monongalia's chief pathologist was not convinced. *"I couldn't believe it. A melanoma 20cm in size with negative nodes and no evident metastatic disease would be highly unlikely."*

The pathologist then ordered a THEROS CancerTYPE ID test. The results of this molecular classification test statistically ruled out melanoma with a 95 percent confidence level and predicted malignant fibrous histiocytoma (which had been part of Monongalia's initial differential diagnosis). *"We were in a difficult position of needing to treat this patient appropriately and quickly, yet a world expert reference laboratory had rendered a diagnosis that we didn't agree with,"* said the chief pathologist.

Monongalia shared the THEROS CancerTYPE ID test findings with the reference laboratory; the laboratory subsequently changed their diagnosis of melanoma to malignant tumor consistent with poorly differentiated sarcoma focally producing melanin. The treatments for this sarcoma and melanoma are very different – the latter being significantly more toxic.

*"THEROS CancerTYPE ID allowed this patient to be categorized correctly and receive appropriate therapy,"* said Monongalia's chief pathologist. *"In addition, we now had a totally different prognosis for this man."*



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## Patient & Order Information

Order ID:  
Patient Name:  
DOB:  
Medical Record #:  
Sample ID:  
Date Received:

Sex: Male  
Site of Biopsy: Chest Wall  
Date of Collection:  
Date Reported:

## THEROS CancerTYPE ID<sup>®</sup> Molecular Cancer Classification Test

**Sample quality:** Sufficient

**Microdissection:** No

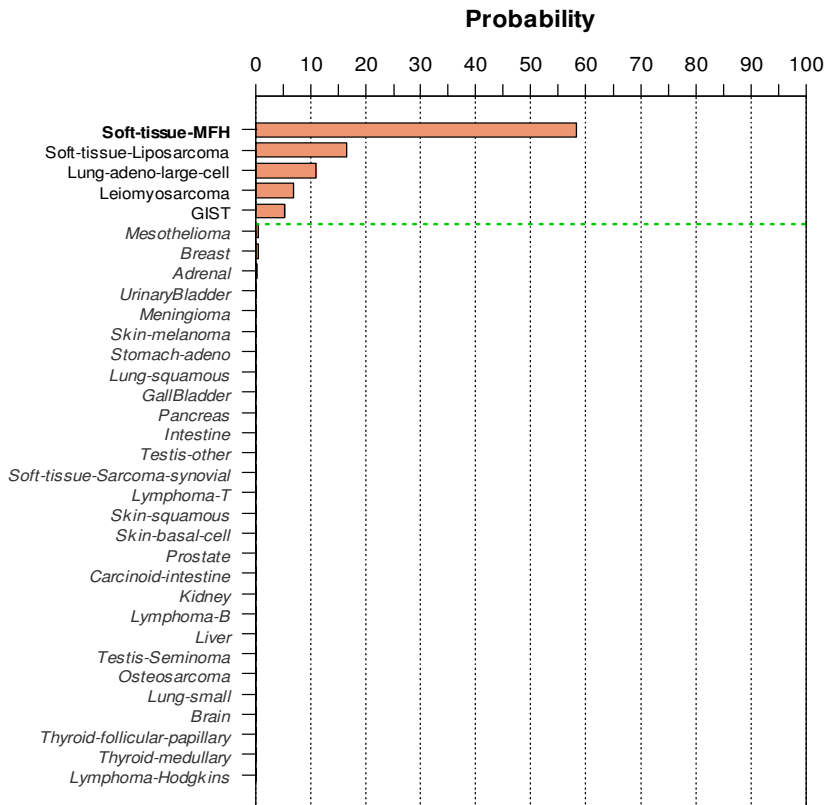
Cancer Type	Probability
Soft-tissue-MFH	58.2%

**Soft-tissue-MFH** 58.2%

### Additional Test Information

The test sample is most similar to the cancer type listed in the table above. The probability is a direct measure of the confidence for the prediction. Other types to consider include: Soft-tissue-Liposarcoma and Lung-adeno-large-cell, which will cover a cumulative probability of 85.8%.

**How it works.** The probability for each cancer type is based on the 92-gene expression profile of the test sample. The probability scores for all cancer types sum to 100%. The cancer type with the highest probability represents the most likely type. When the difference between the highest and the second highest probability is small, the top two or three types are listed as predictions to reach >80% cumulative probability.



**Note: cancer types below the horizontal dashed line are ruled out with 95% confidence. Clinical correlation is recommended for cancer types above this line.**

### Intended Use

THEROS CancerTYPE ID<sup>®</sup> is a molecular test that is recommended to guide the process of cancer classification.

### Test Description and Methodology

This test identifies the most likely tumor origin based on the expression profiles of 92 genes analyzed by RT-PCR and is capable of classifying up to 39 tumor classes. The 92-gene expression profile is obtained by extracting mRNA from tumor-enriched sections of formalin-fixed paraffin embedded (FFPE) tissue and performing real-time quantitative RT-PCR using Taqman<sup>™</sup> technology. This RT-PCR based test has been shown to have an accuracy of 86% in classifying 39 cancer types[1,2]. However, cancer types outside of these 39 types may be unclassifiable or potentially misclassified.

1. Ma et al. *Molecular Classification of Human Cancers Using a 92-Gene Real-Time Quantitative Polymerase Chain Reaction Assay.* *Archives of Pathology and Laboratory Medicine.* 2006;130:465-473
2. Data on File, Technical Report 051909, bioTheragnostics, Inc.

**Laboratory Director:** Bernard S. Chang, M.D.      **CLIA #** 05-D1065725      **CA #** CLF334843

This test was developed and its performance characteristics determined by bioTheragnostics, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. How this information is used to guide patient care is the responsibility of the physician. This molecular cancer classification predictive testing should be interpreted in the context of additional clinical and/or histopathological findings and not in lieu of such studies.