Using MALDI-TOF MS to Screen for Monoclonal Proteins in Serum

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Background: The current clinical methods for identifying monoclonal proteins (M-proteins) in serum include gel protein electrophoresis (PEL) and gel immunofixation electrophoresis (IFE). These methods depend on detecting a restricted migration pattern of the M-protein which is distinct from the polyclonal background. Due to the differing sensitivities of PEL and IFE, current recommendations by the International Myeloma Consortium state that both methods should be used to rule out the presence of an M-protein. Matrix assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) is currently used in the clinical laboratory for identification of microorganisms and genetic variants. This study aims to evaluate MALDI-TOF MS as a clinical screening method for M-proteins in serum**.**

Methods: Five hundred fifty six (556) serum samples that had been previously analyzed by current clinical PEL/IFE testing were evaluated by MADLI-TOF MS (Microflex LT, Bruker Daltonics). The sample set contained 217 IgG, 105 IgA, 73 IgM, 5 IgD , and 11 free light chain M-protein positive sera and 126 negative sera. Prior to analysis, intact immunoglobulins were isolated from serum with Capture Select^{TM} (Hu) LC-kappa and LC-lambda affinity resin (Life Technologies) and reduced with tris (2-carboxyethyl) phosphine hydrochloride (TCEP-HCl,Thermo Scientific). Purified samples were prepared for MALDI-TOF MS analysis using dried droplet method and α-cyano-4-hydroxycinnamic acid as matrix. Mass analysis was performed in positive ion mode with summation of 500 laser shots.

Results: For spectral analysis, the ion distribution of the MH+1 and MH+2 charge states of the light chain were compared to the spectrum of normal serum. Any light chain mass distributions which showed deviations from the normal distribution were considered screen positive. Of the 556 samples assayed, abnormal distributions were identified in 406 of 421 samples (96%) that were positive by PEL/IFE. Abnormalities were also noted in 25 of 135 samples (19%) that were negative by PEL/IFE. Of the 257 samples that were positive by PEL alone, 100% were positive

by MALDI-TOF MS. Of the 164 samples that were positive by IFE only, 149 were positive (91%) by MALDI-TOF MS.

Conclusion: These results suggest that the MALDI-TOF MS method has near equivalent sensitivity to the current PEL/IFE methods. MALDI-TOF MS shows promise as a clinical screening method for M-proteins. Based on current estimates, roughly 70% of sera sent for testing are negative for monoclonal abnormalities by PEL/IFE. Using MALDI-TOF MS as a screening method would result in significant cost savings by reducing the number of samples requiring further follow-up testing.