

Abstract

Approximately 30 percent of inflammatory bowel disease (IBD) patients cannot be accurately diagnosed. As a result, these patients may be prescribed ineffective medical or surgical treatments. The research of Dr. M'Koma is focused on improving the diagnosis for patients with the predominantly colonic IBD subtypes of ulcerative colitis (UC) and Crohn's colitis (CC). When the diagnostic classification for these two diseases is inconclusive, the condition is termed indeterminate colitis (IC). Here, the central medical challenge is the discrimination of IBD into the specific subtypes with high accuracy because it greatly effects medical and surgical care of patients. Diagnostic accuracy of IC into either UC or CC is of utmost importance when determining a patient's candidacy for surgery. Further, incorrect diagnosis and treatment carry potential morbidity from inappropriate and unnecessary surgery.

To address IBD diagnosis accuracy in clinical settings, we are developing a proteomic signature to discriminate between UC and CC patients that will also predict the outcome of IC patients for their eventual progress to either UC or CC. In our preliminary studies, matrix-assisted laser desorption/ionization (MALDI) mass spectrometry was able to distinguish CC and UC specimens on a small set (n=40) of mixed CC and UC biopsies. The technology approach correlates imaging mass spectrometry (IMS) and histopathology to relate novel molecular findings obtained through IMS to the well-characterized and validated histopathology knowledge base. The quality of this correlation between these two modalities is obtained through registration of the two image types.

In the next phase of this research, we will develop novel workflows for MALDI IMS-to-microscopy data registration and analysis using nondestructive IMS-compatible wide field autofluorescence (AF) microscopy combined with computational image registration. Further, analyses and protein identification of the differential proteins will be performed to aid in accurate diagnosis of IBD and point to potential personalized therapies. To test this diagnosis technique against previously known patient outcomes, Dr. M'Koma and his clinical colleagues have collected over 1300 IBD and non-IBD (control) patient colectomy tissue samples with 542 corresponding sera distributed by race and gender including medical data pertaining to patient demographics, variables prior to and after surgery, surveillance endoscopic and clinical findings, and medical and surgical treatment history.

If successful, widespread use of this technology would provide accurate diagnosis and the correct treatment regimens for IBD patients, improving health outcomes and quality of life while reducing medical complications and unnecessary health care costs.