

Autoradiography, MALDI-MS, and SIMS-MS Imaging in Pharmaceutical Discovery and Development

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Whole-body autoradiography (WBA) or quantitative WBA (QWBA), microautoradiography (MARG), matrix-assisted laser desorption/ionization mass spectrometric imaging (MALDI-MSI), and secondary ion mass spectrometric imaging (SIMS-MSI) are high-resolution, molecular imaging techniques used to study the tissue distribution of radiolabeled and nonlabeled compounds in *ex vivo*, *in situ* biological samples. WBA, which is the imaging of the whole-body of lab animals, and/or their organ systems; and MARG, which provides information on the localization of radioactivity in histological preparations and at the cellular level, are used to support drug discovery and development efforts. These studies enable the conduct of human radiolabeled metabolite studies and have provided pharmaceutical scientists with a high resolution and quantitative method of accessing tissue distribution. MALDI-MSI is a mass spectrometric imaging technique capable of label-free and simultaneous determination of the identity and distribution of xenobiotics and their metabolites as well as endogenous substances in biological samples. This makes it an interesting extension to WBA and MARG, eliminating the need for radiochemistry and providing molecular specific information. SIMS-MSI offers a complementary method to MALDI-MSI for the acquisition of images with higher spatial resolution directly from biological specimens. Although traditionally used for the analysis of surface films and polymers, SIMS has been used successfully for the study of biological tissues and cell types, thus enabling the acquisition of images at submicrometer resolution with a minimum of samples preparation.

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