Multi-spectral diagnostic imaging techniques hold unique promise for the acquisition, modeling and subsequent analysis of historic artifacts, capturing surface, sub-surface, volumetric as well as material characteristics. This information, provides a critical step towards establishing the genesis of an artifact as well as its current state of conservation. A major challenge that remains is the accurate calibration and subsequent fusion of the different data assets, and verification of the results. This paper discusses an non-invasive, non-contact, XRF-based approach to analyze the elemental composition of sensitive cultural heritage artifacts, in the context of a painting by Leonardo da Vinci. Specifically, Leonardo da Vinci’s "The Adoration of the Magi" drawing, located at the Gabinetto Disegni e Stampe degli Uffizi, 436 E, Florence, was studied through multi-spectral imaging and unique features identified that were subsequently further studied with XRF, allowing qualitative conclusions to be drawn about the artist’s technique, and a hypotheses to be developed about the materials used, the sequence of execution of various elements in the drawing, and localization of areas re-worked from the original state. The XRF analysis served as an important complementary technique and provided an objective confirmation that supported evidence from the diagnostic imaging analysis. Identification of materials used and the order and method with which they were applied provided critical insight into the progression of design and motifs incorporated in the work by da Vinci, as well as, valuable information for future conservation efforts.