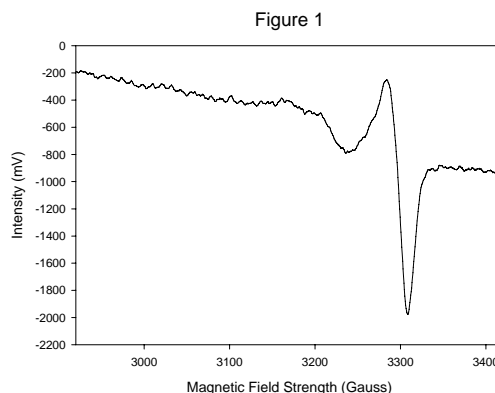


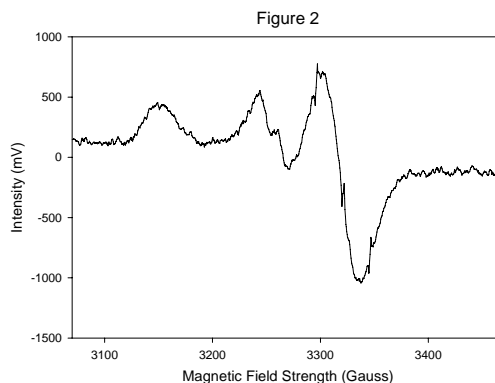
EX VIVO ANALYSIS OF IRRADIATED FINGER NAILS: QUANTIFYING THE RADIATION-INDUCED SIGNAL IN FINGERNAILS IN THE PRESENCE OF AN INTERFERING SIGNAL FROM MECHANICALLY-INDUCED RADICALS

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Radiation-induced (IR) changes in finger nails have the potential to serve as the basis of a biosimetric method in human exposures to ionizing radiation. Specifically, we are exploring the use of ex vivo electron paramagnetic resonance (EPR) measurements of the signal produced from the quasi-stable IR-induced radicals formed in keratins and other nail proteins. A quantitative analysis of the IR radical signal (RIS) shows the presence of at least two components, a singlet at $g = 2.005$ and a broad line centered at ca. 2.026 (Fig. 1). The line at $g = 2.026$ is tentatively attributed to a thiyl radical centered on cysteine. The signals from both the $g = 2.005$ and 2.026 components show a linear dose-response in their peak-to-peak signal intensities to > 200 Gy, with detection sensitivities that are sufficiently low to quantify the RIS at doses that include the clinically relevant range (≥ 2 Gy).



However, because the EPR method uses ex vivo measurements of RIS in nail clippings, there is a signal from mechanically-induced radicals (MIS) generated at the shear edge of the clipping, which interferes with our ability to accurately quantify the RIS signal. The predominant signal that is observed for MIS has g -values of 2.056 (g_z), 2.026 (g_y) and 1.98 (g_x) and is attributed to a perthiyl radical (Fig. 2). This radical likely arises from mechanical scission of the cystine disulfide bonds that are common in nail proteins. Another component of the MIS signal is centered at $g = 2.005$ which interferes with our ability to quantify the RIS signal at the same g -value.



Interestingly, the perthiyl radical is not observed in the RIS signal in nails at doses below 1 kGy. Similarly, the thiyl radical observed in the RIS signal is not observed in the MIS signal at doses below 1 kGy. Therefore, in an effort to more clearly identify and quantify the RIS component of the finger nail signal from the MIS we are devising strategies that takes advantage of these spectral differences. We will describe the results of our method development efforts that will, for example, allow us to take advantage of the differential decay kinetics of the RIS and MIS signals, and/or use a basis set of RIS or MIS specific spectra for spectral deconvolution or internal additions approaches for measuring RIS in the nails.