

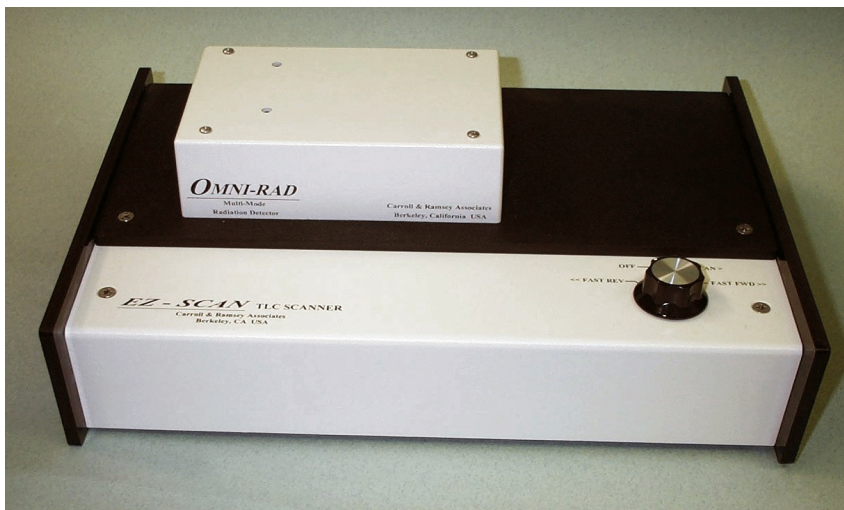
Enhanced Detection of Weakly-Penetrating Alpha Radiation via Thin Layer Chromatography

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Author's note *This is a work-in-progress, initiated shortly before news of a potential pandemic began to be reported. Our abstract was submitted and accepted before public-health and government-mandated lockdowns were imposed. In early March, our collaborator at the University of Utah was locked out of her lab until mid June, preventing her from obtaining much-needed field data. So we have done the best we could with the data we had, under circumstances beyond our control.*

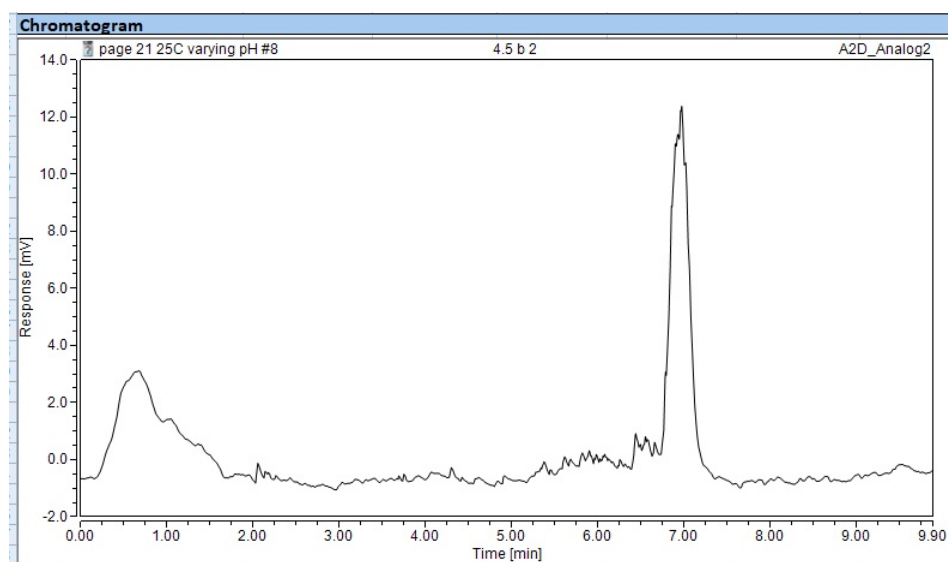
Introduction: Targeted Alpha Therapy is regarded as having potential advantages in the treatment of cancer due to the alpha particle's extremely short range in tissue – on the scale of cellular dimensions – which results in highly localized deposition of energy *in vivo* and consequent tumor-cell killing ability without harming nearby tissue. But this same property renders the alpha-emitters difficult to detect directly with commonly-available instrumentation.

We are developing an enhanced version of our **Omni-Rad** thin-layer chromatography beta-detector module to directly detect alpha-particles. The average energy of an alpha particle is more than an order of magnitude greater than that of photons or beta particles, anticipating correspondingly greater signal-to-noise ratio per unit activity.



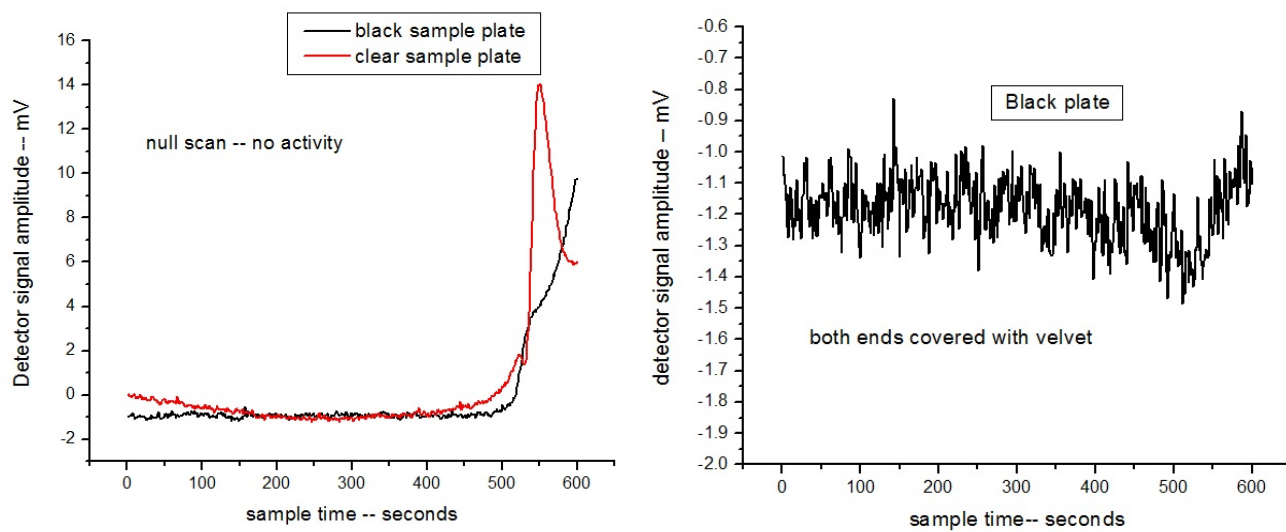
Materials and Methods The active components in our *Omni-Rad* beta-detection module are a 1 cm² Si PIN photo-diode, followed by a trans-resistance (current-to-voltage) amplifier whose gain – expressed in units of ohms – is 3.7×10^9 . The photo-diode is shielded from ambient room light and electromagnetic interference by a 3 mil thick Aluminum foil window covering the detector aperture. However, the combination of a relatively thick foil window and the protective polymer coating on a standard photo-diode are enough to totally block the alpha's so, for our alpha detector prototype, we employed the same trans-resistance amplifier in combination with a special 'window-less' photo-diode¹, along with a much thinner (0.1 mil) Aluminized Mylar window².

Initial results As proof of concept, Dr. Tara Mastren, in the Nuclear Engineering Program at the University of Utah, kindly agreed to road test our prototype detector module and run some trial TLC scans in her lab using the alpha-emitting nuclide ²²⁵Ac. Below is an early result for ~50 nCi free ²²⁵Ac in Ammonium Acetate, 'spotted' onto the TLC plate. The peak at 7.0 minutes (~12 mV) is the ²²⁵Ac.



The initial peak at 0.5 minute is problematic, indicating interference from ambient room light leaking into the detector, which was further confirmed back in our own lab.

Though required to facilitate transmission of weakly-penetrating alpha's, the thin (0.1 mil) Aluminized mylar foil – while appearing opaque when held up to a bright light – isn't truly opaque. Depending on placement of the TLC scanner relative to overhead lighting, our original prototype module would produce some serious artifacts in the scan traces that couldn't be eliminated short of literally covering the scanner with black velvet cloth.



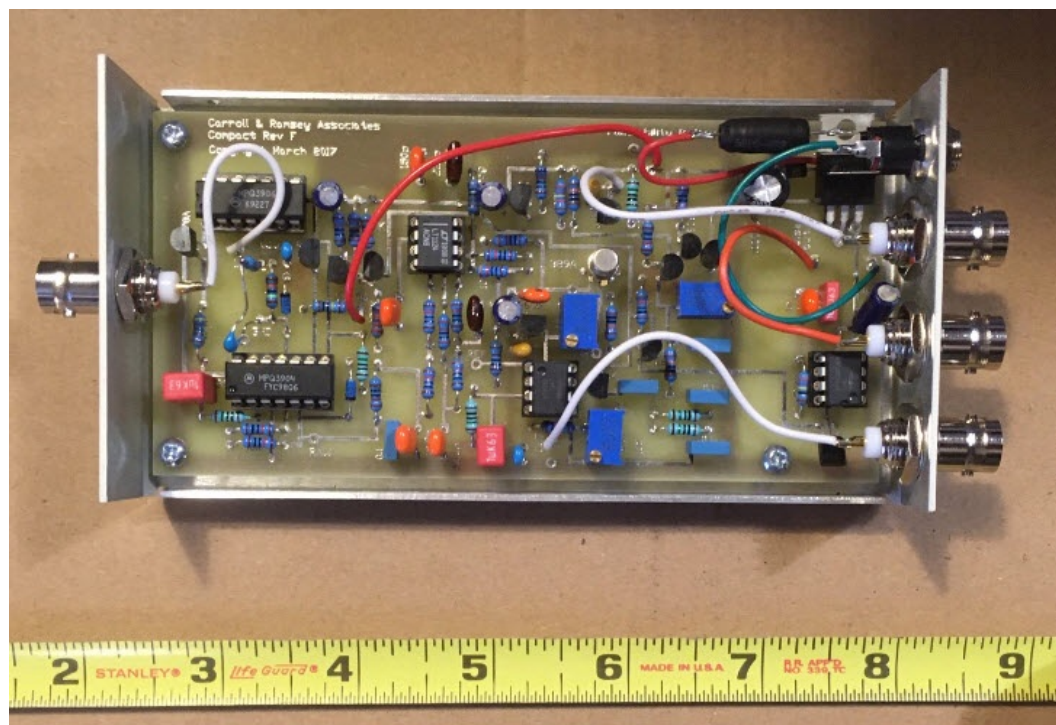
So we turned to an alternative 'pulse-mode' detector system design in which, unlike the initial 'current-mode' prototype, the new scheme has a near-zero signal response to the 'DC' and low-frequency components of daylight and standard fluorescent, LED, or incandescent room illumination.



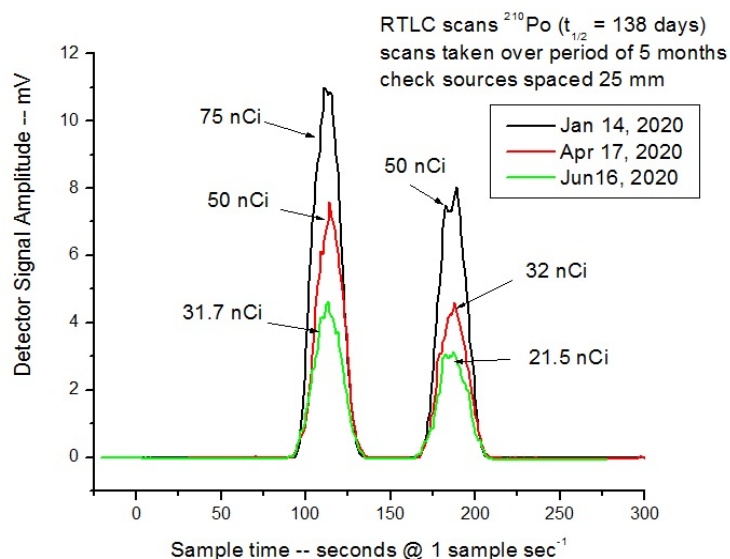
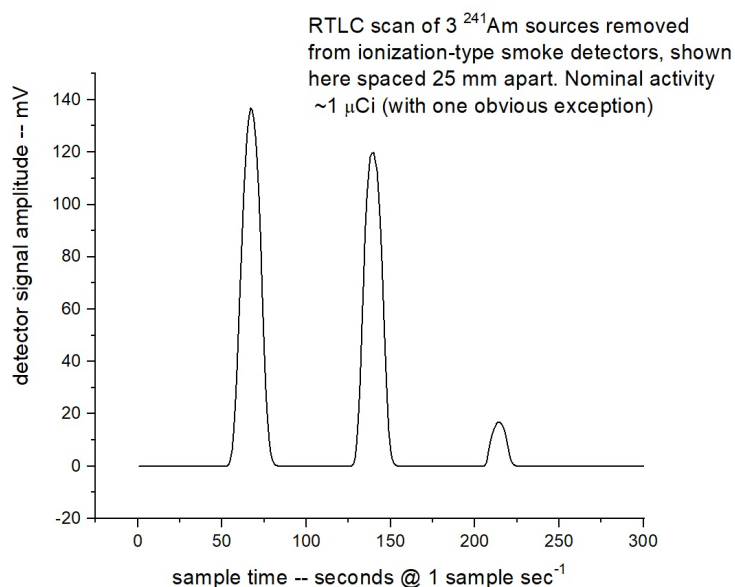
As a practical matter, tucking the new module into its station atop the scanner base, and setting the threshold dis-criminator just above the detector noise floor is sufficient to eliminate all such light-induced interference in a normal lab setting.

Pulse-mode detector The current-amplifying trans-resistance amplifier in the initial alpha detector prototype is inherently linear over a wide range of radiation intensities. But precise readings at very low activity levels may be impaired – even beyond the effects of meager counting statistics – by base-line fluctuation, noise, and drift inevitably present in high-gain ‘current-mode’ photo-diode amplifiers. We reasoned that, in addition to providing greater immunity to ambient room light, a detector operating in ‘pulse - mode’, incorporating a threshold discriminator to eliminate base-line fluctuation and drift, would also provide superior signal-to-noise ratio at the lowest levels of activity ⁴.

The un-painted cast metal box in the figure above contains the windowless Si PIN photo-diode close-coupled to a charge-integrating pre-amplifier⁵, further connected to the signal input of the adjacent chassis box – our Model 105C scintillation detector post amplifier – slightly modified for the present application. The post-amplifier is powered separately from the TLC scanner by a 24VDC ‘wall-wart’ style plug-in adapter.



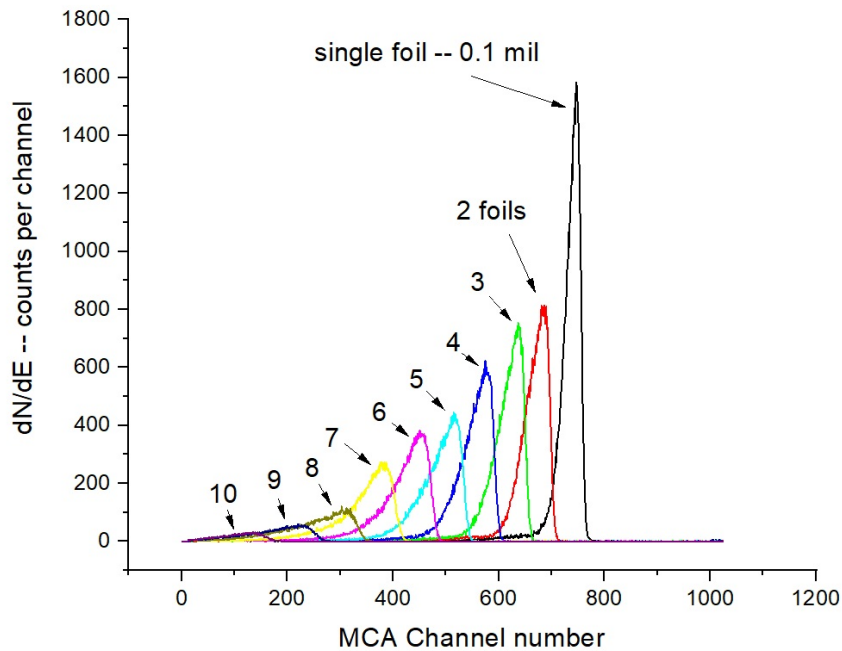
Pulse-mode detector Performance In our own workshop, we do not have the wet-chemistry infra-structure, nor access to alpha-emitting nuclides in a form compatible with performing actual thin-layer chromatography scans, so we are only able to perform ‘mock’ scans using small check sources, as shown below.



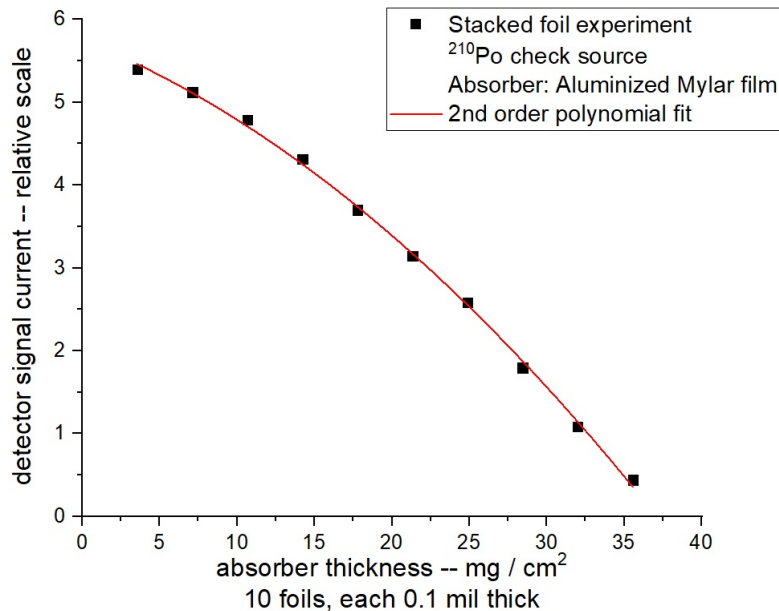
Above: These ‘mock’ TLC traces show an excellent signal-to-fluctuation ratio using our pulse-mode detector module to scan point sources of alpha-emitting activity as low as a few ten’s of nano-curies at a scan rate of 20 mm / min and a detector aperture width of 3 mm.

Reality check But that said, all may not be as we would wish.....Among our early questions and concerns was whether or not the alpha-emitting activity would be ‘buried’, hence rendered less detectable – or even undetectable – within the stationary phase on the TLC test strip.

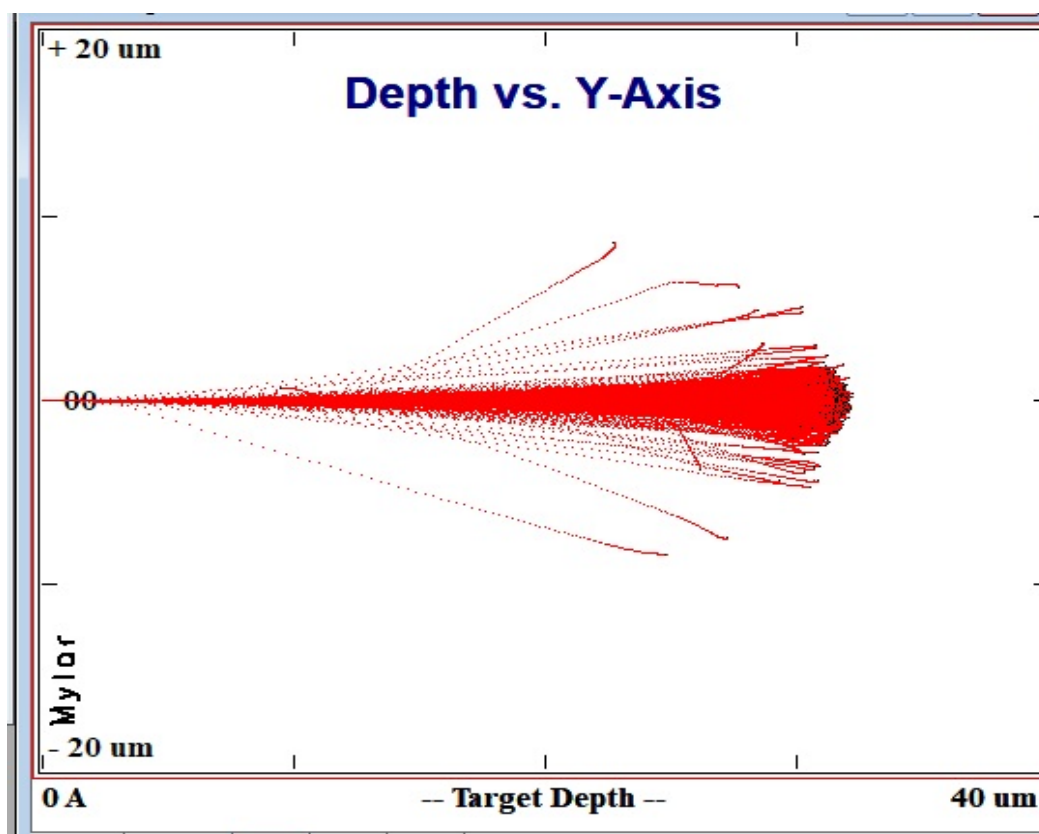
To gain insight into what might be happening within a TLC sample plate, we did a series of ‘stacked foil’ alpha-transmission measurements using thin mylar foils (density $\sim 1.55 \text{ gm} / \text{cm}^3$).



Above: Individual Alpha particle energy spectra from a ^{210}Po check source⁶ whose principal emission is 5.4 MeV. The alpha's penetrate a number of 0.1 mil Mylar foils before being stopped in the Si diode and their energy recorded in a multi-channel analyzer (MCA)



Above: Detector signal current as a function of absorber thickness. Note that the signal current essentially vanishes beyond 10 foils, or ~1 mil ($\sim 3.8 \text{ mg}/\text{cm}^2$) total thickness.



Above: A further check via SRIM computer simulation⁷ confirms that the range of 5.4 MeV alpha's in mylar is slightly over 30 microns (~1.2 mils)

Additional SRIM simulation runs on materials commonly used on TLC plates – silica and alumina – assuming the same material density of 1.55 gm / cm³, yielded a range just over 35 microns for each.

The stationary phase on typical TLC sample plates is of the order of 4 to 10 mils (100 - 250 microns) deep. If we assume the latter (250 microns) and a uniform distribution of activity throughout the full depth of the sample layer, that would mean that up to 90% of alpha-emitting activity is buried, and thus undetectable.

The TLC sample plates used in the initial field trials at the University of Utah are Agilent type iTLC-SG⁹ measuring 333 microns thick, with a bulk density of 0.25 gm / cm³. The alpha-emitting nuclide, ²²⁵Ac (E_{α} = 5.8 MeV, $T_{1/2}$ = 9.92 days) is in equilibrium with three short-lived alpha-emitting daughters⁸

²²¹Fr (E_{α} = 6.4 MeV, $T_{1/2}$ = 4.8 min);

²¹⁷At (E_{α} = 7.1 MeV, $T_{1/2}$ = 32.8 ms);

²¹³Po (E_{α} = 8.4 MeV, $T_{1/2}$ = 3.7 μ s) following β^{-} decay of ²¹³Bi ($T_{1/2}$ = 45.6 min)

resulting in a total alpha-energy per ²²⁵Ac decay of ~27.7 MeV.

We compared the detector responses between our ‘mock’ scan using unsealed (hence un-attenuated) ²¹⁰Po check sources versus the ‘real’ RTLC scan done at the Utah lab using ²²⁵Ac. For a known amount of activity in each of the samples, the responses are expressed in units of mV-seconds (i.e., area under the RTLC peaks) divided by (MeV / second) emitted by the respective nuclides.

The result: ²²⁵Ac yielded 4.5×10^{-3} mV-seconds per MeV/second;

²¹⁰Po yielded 0.14 mV-seconds per MeV/second.

The ratio, ²²⁵Ac / ²¹⁰Po = 0.032, indicates that there is indeed significant loss of signal response due to attenuation in the ²²⁵Ac scan.

The way Forward The most obvious way to improve detection efficiency would be to use TLC sample plates with the thinnest practical stationary phase. The Agilent TLC plate used with ²²⁵Ac, with its substantially lower bulk density (0.25 gm/cm³) relative to our earlier assumption of 1.55 gm/cm³, is leading in the right direction and clearly yields a useful signal, further enhanced by a reduction in statistical fluctuation (4 alpha’s per decay) as compared to alpha-emitting nuclides with only a single alpha particle per decay. Further study is required in order to better understand the above-cited, and seemingly excessive degree of attenuation.

Post Script As of June 18, 2020: Dr. Mastren is finally back in her lab! When we spoke by phone she raised an interesting and intriguing point. Her TLC trace cited earlier was done using free ^{225}Ac in Ammonium Acetate which, evidently, is distributed throughout the full thickness of the TLC plate.

However, the focus of her research is to explore the possibility of embedding the ^{225}Ac in Si nano-particles³ in order to constrain the daughters – particularly the longer-lived nuclides such as ^{221}Fr and ^{213}Bi – which are ejected from the ^{225}Ac labeled chelate and could otherwise wander freely throughout the body.

It is likely – though not tested at the time of this writing – that the nano-particles, being relatively large (~200 nm), would not penetrate into the bulk material of the TLC plate – instead staying on the surface and thus not being affected by attenuation. However, daughters that do break free of confinement could ‘go deep’, leading to different detector responses for different component peaks! This general concept is discussed in the chromatography literature in the context of low-energy Beta detection^{10, 11}. All of which will obviously require further study...

References

- 1) Hamamatsu Photonics <<https://www.hamamatsu.com>>
- 2) Goodfellow Metals <www.goodfellow.com>
- 3) Mastren, T; *Increasing Precision in Cancer Cell Death to Prevent Metastasis* <<https://netrf.org/2019/04/16/targeted-alpha-therapy-for-nets>>
- 4) L. Carroll; *Achieving a Linear Dose-rate Response in Pulse-Mode Silicon Photodiode Scintillation Detectors Over a Wide Range of Excitations.* <<https://www.worldscientific.com/doi/pdf/10.1142/S2010194514601367>>
- 5) US Patents: 5,990,745; 6,054,705; 9,081,102 B2

6) Spectrum Techniques, Oak Ridge, TN;

<<http://www.spectrumtechniques.com/products/sources>>

7) **SRIM** – Stopping and Range of Ions in Matter; Tutorials and Simulation software for download at <[srim.org](http://www.srim.org)>

8) Suliman, Pomme, Mouruli, et al; '*Half Lives of ^{221}Fr , ^{217}At , ^{213}Bi , ^{213}Po and ^{209}Pb from the ^{225}Ac decay Series*'. Applied Radiation and Isotopes (77) 2013 pp.32-37.

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11) Filshuth, Heinz. Chapter 4; *Detection of Radiochromatograms and Electropherograms with Position-sensitive Wire Chambers*; Op.Cit

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