Primary measurement methods for the determination of absorbed dose and activity of alpha-emitting radionuclides

Sean P. Jollota[1], Denis Bergeron[2], Ahtesham Khan[1,3], Jeffrey Radtke[1], Larry DeWerd[1]

[1] Department of Medical Physics, University of Wisconsin, Madison, WI, 53718
[2] National Institute of Standards and Technology, Gaithersburg, MD, 20899
[3] Northwestern Memorial Hospital, Northwestern University Feinberg School of Medicine, Chicago, IL, 60611

In the early 2000s, there was a resurgence of the use of alpha-emitting radionuclides for therapeutic applications due to the adaptation of Radiopharmaceutical Therapy (RPT) to use these sources [1]. In the dosimetry workflow for these applications, activity is measured before administration to the patient. Quantitative imaging at specific time points after the administered activity is used to quantify standardized uptake values (SUV) that are correlated to the time-integrated activity (TIA). The TIA is converted to absorbed dose using computational methods [2]. These computation methods are based on radiation transport models, interaction cross-sections, and nuclear decay and emission input data that can drastically change the resulting absorbed dose [3]. This work investigated the development of a measurement procedure to standardize the same source for both activity and absorbed dose to include a traceable absorbed dose quantity for RPT applications.

From a solution of radioactivity with the highest possible activity concentration, a dilution is measured using the Triple to Double Coincidence Ratio (TDCR) method of Liquid Scintillation (LS) counting [4]. The TDCR method affords an absolute determination of LS counting efficiency for a primary realization of the becquerel in terms of massic activity. The quantification of the absorbed dose is measured from an evaporated drop on a nickel disc. The massic activity is directly linked via gravimetric dilution factors to the solution that is drop casted on the nickel disc. The spatial location and homogeneity are quantified with images collected with the ionizing-radiation Quantum Imaging Detector (iQID). The self-attenuation within the evaporated deposit is assessed using the acquired alpha spectra analysis.

Extrapolation chamber components are currently being compiled for the NIST Dosimetry group based on an existing chamber at the University of Wisconsin–Madison. Some of these components include a Hexapod motion stage that can translate about six axes, Printed Circuit Board (PCB) electrode, Capacitance to Digital Converter (CDC), programmable high voltage supply, and electrometer. The hexapod and PCB electrode are shown in Figure 1. Measurement in this chamber consists of several steps. The first is the alignment of the collecting electrode to the substrate. This consists of a lateral positional scan to find the maximum charge readout. Next is the tilt alignment, which consists of converting the collecting electrode to use the segmented guards for readout. These guard sectors are connected to the CDC, which also provides an excitation pulse to the substrate. The substrate is tilted until the differential capacitance between opposing sectors is minimized, thereby ensuring parallelism with respect to the collecting electrode. The coordinate system of the hexapod is locked to allow for translation normal to the top surface of the substrate. The diameter of the collection volume and the air gap distance between the collecting electrode and the substrate is then determined. Under the assumption that the cavity created by the electric field between the substrate and the collecting electrode acts as a parallel-plate capacitor, equation (1) can be used to solve for the air gap distance between the substrate and collecting electrode, $\mathrm{l_{offset}}$, and the cavity area, $\mathrm{A_{eff}}$.

$$\mathrm{l_{assumed}} = \frac{\epsilon_r \epsilon_0 \mathrm{A_{eff}}}{\mathrm{C}} + \mathrm{l_{offset}} \tag{1}$$

ϵ_r is the dielectric constant of air, ϵ_0 is the permittivity of vacuum, and $l_{assumed}$ is the assumed air gap distance. Using the programmable high voltage supply and a custom Python script used to control the electrometer, hexapod, and voltage supply, measurements are taken at multiple air gaps. The electrometer samples unfiltered current at 10 Hz as the substrate voltage is changed from -10 V to -100 V. The resulting displacement current is then converted to capacitance. Capacitance is measured at five air gaps, and a linear fit is applied to the results to obtain the l_{offset} and A_{eff} shown in equation (1). After the A_{eff} is measured with the non-plated substrate, only the l_{offset} is determined for subsequent measurements of the capacitance after the source has been plated on the substrate. Figure 2 shows the plot of the displacement current with the subtracted background, where the total displacement charge is time-integral of the current recorded between zero and 2.4 seconds.

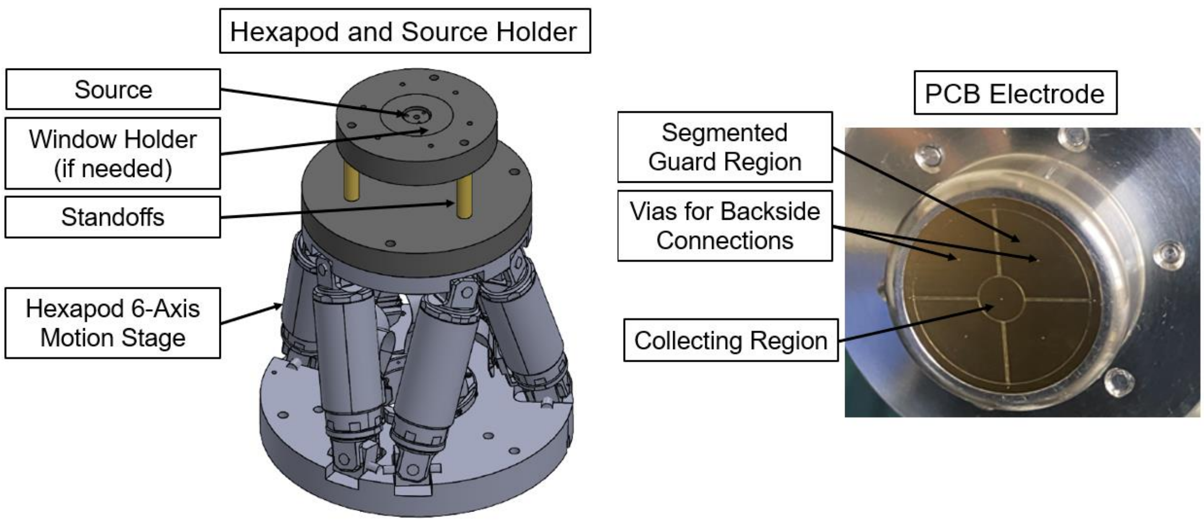

Figure 1. Image of the Hexapod motion stage (left) and the PCB electrode (right).

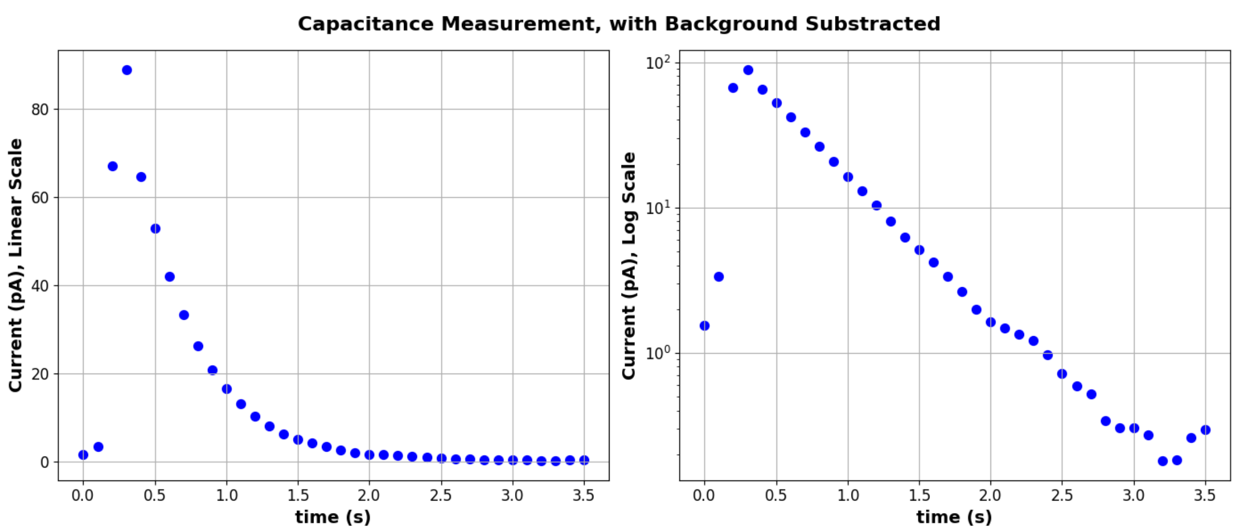

Figure 2. Measured displacement current after the applied change in voltage.

With the source aligned and the air gap distance known, measurements are taken to determine the electric field strength needed to minimize the effects of recombination. Due to the higher Linear Energy Transfer

(LET) of alpha particles, initial and general recombination need to be accounted for. Equation (2) shows the recombination correction used:

$$\frac{1}{Q} = \left(\frac{1}{Q_{sat}} + \frac{\alpha}{V} + \frac{\beta}{V^2}\right) e^{-\gamma V} \tag{2}$$

Where α, β, and γ are fitting parameters, Q_{sat} is the saturation charge, Q is the charge collected, and V is the applied voltage. The recombination correction is acquired using multiple applied voltages, and the results are fit to equation (2) and optimized using a least squares fit. The applied voltages are between 3 and 300 V and an example result is shown in Figure 3. This determines the electric field strength required to minimize this correction.

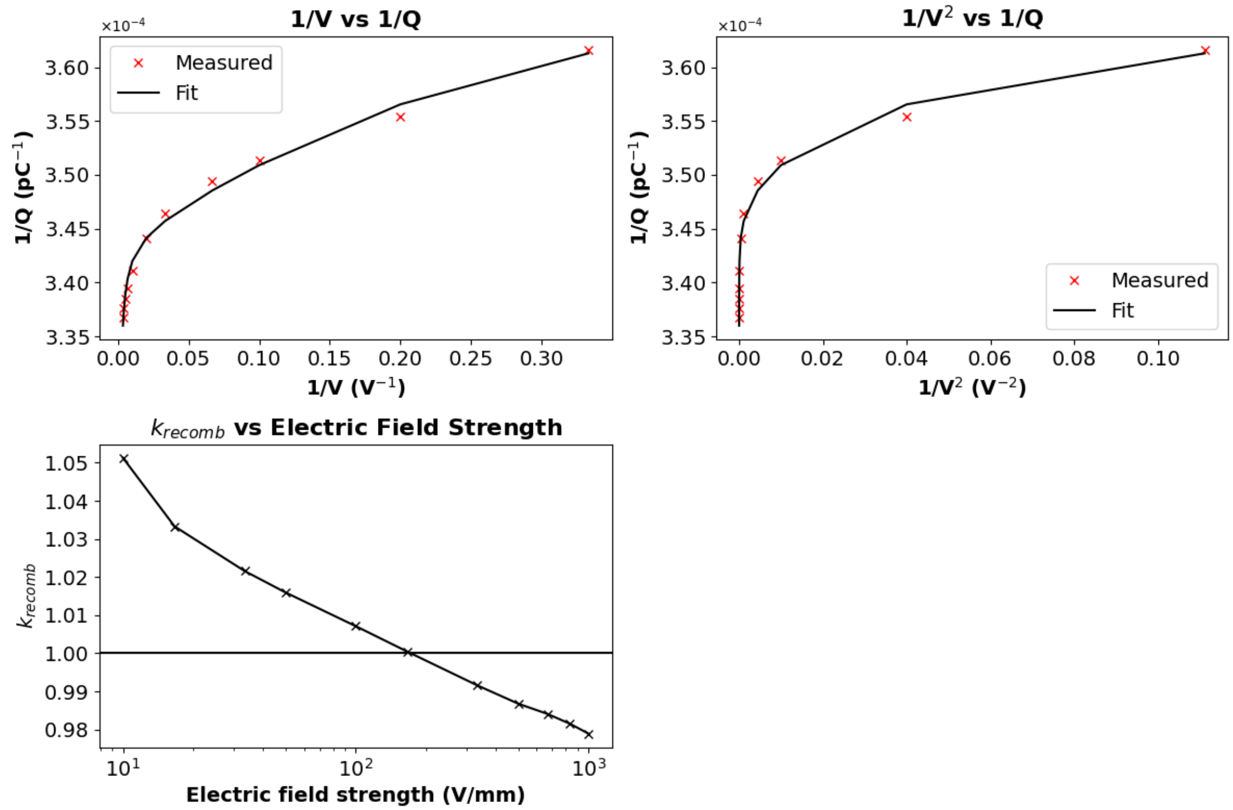

Figure 3. Plotting of 1/V (top left), $1/V^2$ (top right), and Recombination Correction (bottom).

Extrapolation measurements are taken at air gap intervals between 300 and 1000 μm; results of current per activity are shown in Figure 4. These results are corrected and fitted to extrapolate to the absorbed dose at the surface of the substrate. Combining these results with the activity determination results in an absorbed dose per activity quantity. The primary determination of absorbed dose per activity can be compared against the computational methods currently utilized in the RPT dosimetry workflow to convert from TIA to absorbed dose to standardize the absorbed dose quantity.

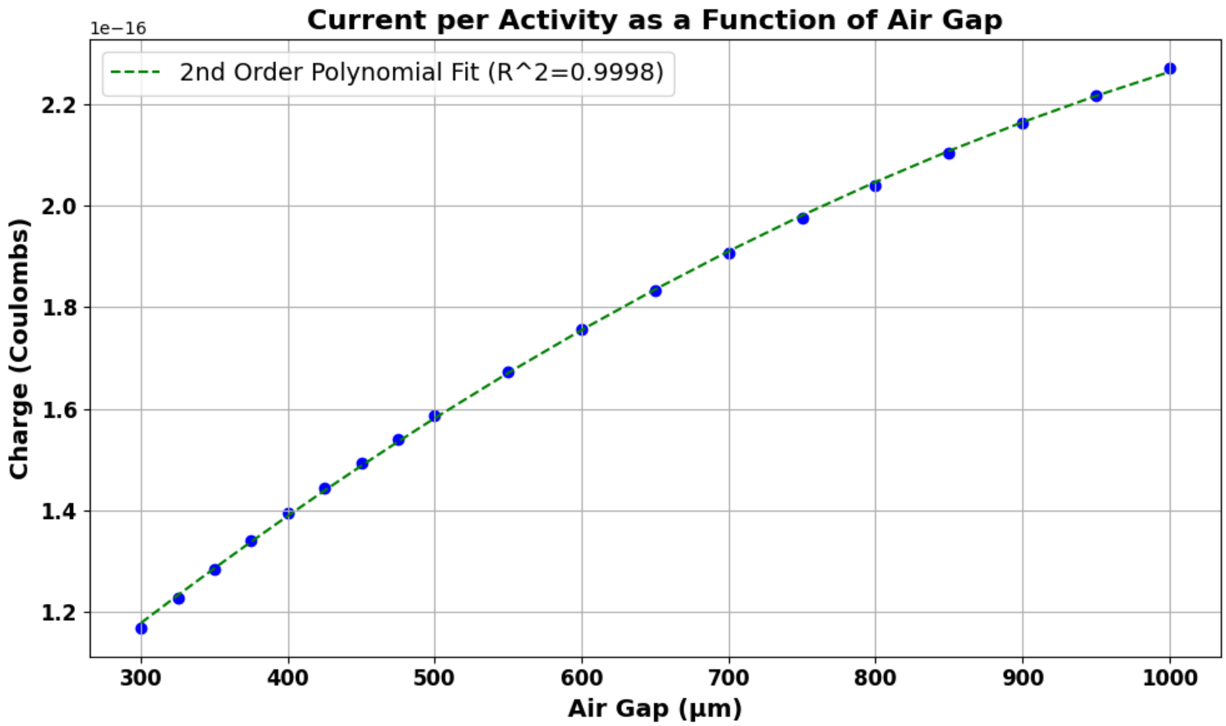

Figure 4. Results of current per activity as a function of the air gap.

Relevance to CIRMS: Establishing an absorbed dose standard will help quantify both source strength quantities used in RPT applications. This will help standardize one step in the RPT dosimetry workflow, where several other steps still need to be better standardized. Hopefully, this work is a step towards a complete traceability of the RPT dosimetry formalism.

References:

1. Mulford DA, Scheinberg DA, Jurcic JG. The Promise of Targeted-Particle Therapy. J Nucl Med 2005;46:199–204.

2. Danieli R, Milano A, Gallo S, Veronese I, Lascialfari A, Indovina L, et al. Personalized Dosimetry in Targeted Radiation Therapy: A Look to Methods, Tools and Critical Aspects. J Pers Med 2022;12(2).

3. Billas I, Shipley D, Galer S, Bass G, Sander T, Fenwick A, et al. Development of a primary standard for absorbed dose from unsealed radionuclide solutions. Metrologia 2016;53(6):1259–71.

4. Bergeron DE, Kossert K, Collins SM, Fenwick AJ. Realization and dissemination of activity standards for medically important alpha-emitting radionuclides. Applied Radiation and Isotopes 2022;184.