
by

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Thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in the Graduate Program in Medical Physics in the Graduate School of Duke University

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ABSTRACT


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Abstract

Project 1: Chest Phantom Development for Chest X-ray Radiation Protection Surveys

Purpose: Develop an acrylic phantom to accurately represent an average adult’s chest for use in radiographic chest unit radiation protection surveys.

Materials and Methods: 6 sheets of 3.81 cm thick acrylic were cut and assembled to form a 30.5 x 30.5 x 20.3 cm hollow box phantom. The acrylic served as tissue equivalent material and the hollow center simulated lungs in a human patient. Six sheets of 1 mm thick aluminum were cut to line the inner walls of the acrylic phantom to potentially boost scatter radiation. Three phantoms underwent posterior-anterior (PA) and lateral chest protocol radiographic scans: the acrylic phantom (with and without the aluminum lining), a 3 gallon water bottle filled with water, and an adult male anthropomorphic phantom. The phantoms were set up as though they were adult patients and scanned with automatic exposure control. Scatter radiation was measured with ion chamber survey meters at 4 points within the room for each phantom and protocol. The scatter data from the acrylic phantom and water bottle were compared to the anthropomorphic phantom to determine which one more accurately represented an adult patient.

Results: For the PA protocol, the average percent difference in measurements between the acrylic phantom and anthropomorphic phantom was $33.3 \pm 28.8\%$ with the...
aluminum lining and 33.0 ± 21.2% without the lining. The percent difference between the water bottle and anthropomorphic phantom was 66.5 ± 42.0%. For the lateral protocol, the average percent difference in measurements between the acrylic phantom and anthropomorphic phantom was 157.6 ± 5.6% with the aluminum lining and 143.0 ± 17.6% without the lining. The percent difference between the water bottle and anthropomorphic phantom was 78.3 ± 22.8%.

**Conclusions:** The acrylic phantom provided a more accurate comparison to the anthropomorphic phantom than the water bottle for the PA protocol. For the lateral protocol, neither the acrylic phantom nor water bottle provided an adequate comparison to the anthropomorphic phantom.

**Project 2: Internal Beta Dosimetry of an Iodine-131 Labelled Elastin-Like Polypeptide**

**Purpose:** Develop a model and simulation to better understand the dosimetry of an I-131 labeled elastin-like polypeptide (ELP) brachytherapy technique.

**Materials and Methods:** To develop the model, an average scenario based on mouse trials was explored. A 125 mg tumor was approximated as a sphere, with the I-131 ELP injected into its center. The ELP solidifies into a spherical depot – approximately 1/3 the volume of the tumor – and becomes a permanent brachytherapy source. The injected activity of I-131 was 1.25 mCi. I-131 primarily emits β radiation with an average energy
of 182 keV, therefore it was determined that all such emissions were confined within the bounds of the tumor. Gamma emissions associated with I-131 were ignored as they were determined to have enough energy to escape the bounds of the tumor without any interaction. This model was implemented into a simulation using the Monte Carlo program FLUKA. From this simulation, the absorbed dose to the tumor and ELP depot, along with the dose profile, was calculated.

**Results:** The tumor received an absorbed dose of 72.3 Gy while the ELP received $1.14 \times 10^3$ Gy. From the dose profile, it was determined that 99% of the absorbed dose to the tumor was highly localized to a 0.3 mm region surrounding the ELP depot.

**Conclusions:** The model and simulation provided a better understanding of the dosimetry underlying the novel ELP brachytherapy technique. Results obtained demonstrated that the ELP method delivers doses that are comparable to current conventional brachytherapy techniques.

**Project 3: I-131 Beta Detection Using a Scintillating Nanoparticle Detector**

**Purpose:** Determine if a scintillating nanocrystal fiber optic detector (nano-FOD) could detect β emissions from I-131.

**Materials and Methods:** The nano-FOD’s β response was tested using a source vial containing 101 mCi of I-131 in 2 mL of stabilizing solution. A glass vial containing the I-
131 was placed inside a lead pig for shielding. A 1 mm diameter hole was drilled through the tops of the vial and pig to allow insertion of the nano-FOD. Measurements were taken every day over a 17 day period by repeatedly submerging the nano-FOD in the I-131 solution and recording the voltage signal it produced. The activity at the time of measurement was calculated based on the time and date of data acquisition. The net signal and signal-to-noise ratio (SNR) were then calculated and plotted as functions of I-131 concentration.

**Results:** The nano-FOD produced a measurable response when exposed to the $\beta$ emissions of I-131. The net signal and SNR both demonstrated a linear correlation with the concentration of I-131.

**Conclusions:** The nano-FOD was demonstrated to be capable of $\beta$ detection with a linear correlation to activity. If the signals measured can be calibrated to radiation exposure, then the nano-FOD has promising applications as a novel $\beta$ detector.
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Introduction

Project 1

State regulations require that radiation protection surveys be performed to ensure chest x-ray rooms have adequate shielding to reduce occupational and public exposure to tolerable limits. These surveys are performed whenever a new unit is installed or modifications are made to the room or machinery. To test the unit and ensure adequate wall shielding, phantoms are exposed and survey meters are used to measure the resulting scatter radiation both inside and outside the room. The phantoms used in such surveys must represent an average human to ensure that similar amounts of scatter radiation are produced. If a phantom fails to accurately represent a human, then the amount of radiation measured during a survey may be inaccurate, resulting in inadequate shielding.

The current standard operating procedure (SOP) for medical x-ray radiation surveys at Duke specifies the use of a 1 gallon water bottle filled with water when surveying radiographic units [1]. The water bottle is positioned in the radiation field as though it were a patient and the radiographic unit is operated under worst case scenario conditions [1]. These conditions include higher than normal voltages (kVp), milliampere seconds (mAs), and scan times. During a single exposure – typically 2 seconds in duration – an ion chamber set to rate mode is used to measure the maximum exposure
rate in μR/hr [1]. These measurements are taken at multiple positions around the room to determine the positional variation of scatter radiation [1].

Several questions arose about the current SOP, primarily regarding the use of a 1 gallon water bottle for radiographic unit surveys. This size was chosen for such surveys because it was assumed to match the dimensions of an average adult’s chest and, by extension, produce similar amounts of scatter radiation. Realistically, the 1 gallon water bottle more closely resembles the dimensions of a pediatric patient rather than an adult. This led to concerns that the measured exposure rates could be underestimated due to inaccurate adult human representation. The use of non-clinical exposure conditions also posed issues, as the high kVp settings required that the detector assembly be moved out of the radiation field to avoid oversaturating or damaging the digital detector electronics. This would result in a setup where scatter radiation from the bucky was not included in measurements.

To address these technical questions regarding the use of a water bottle in chest x-ray unit surveys, an acrylic phantom was developed to simulate an average adult’s chest. This phantom, along with a 3 gallon water bottle, was then compared to a ‘gold standard’ adult anthropomorphic phantom in a radiographic scatter radiation survey. All phantoms were scanned according to clinical protocols, providing a realistic setup that included the bucky. The results from this survey were then used to determine
which phantom provided a more accurate comparison to the anthropomorphic
phantom.

**Project 2**

Brachytherapy is a treatment method in which sealed radioactive sources are
used to deliver highly localized radiation to a tumor [2]. These sources can be implanted
directly into a tumor (interstitial), inserted into a cavity (intracavitary), or applied to a
surface [2]. Prostate cancer is the most common disease to undergo brachytherapy
treatment, with up to 40% of patients undergoing the procedure over other treatment
options (prostatectomy or external beam therapy) [2, 3]. Two forms of brachytherapy
implants exist for prostate cancer: high-dose rate temporary implants and low-dose rate
permanent seed implants [2]. Prostate cancers undergoing brachytherapy are
predominantly treated with permanent implants which are left in the patient forever
and pose no significant hazard to the surrounding environment [2, 3]. Interest in
brachytherapy has renewed over the past few decades due to the introduction of new
radioactive sources, application techniques, and technology which reduces personnel
exposure [2, 3].

Although brachytherapy has proven to be an efficacious treatment method for
prostate cancer, current permanent seed implants have their limitations. Such implants
are limited to low- to intermediate-risk malignancies and may cause physical and
psychological discomfort in patients [3]. A polymer-based approach to brachytherapy
has been sought after to overcome the limitations of seed implants, but such methods have been plagued by unique issues of their own – primarily, poor retention and off-target toxicity due to degradation [3].

Schaal et al. have developed a brachytherapy method utilizing thermally sensitive micelles composed of an elastin-like polypeptide (ELP) labelled with iodine-131 (I-131) [3]. At temperatures below 21° C, the radioactive ELP micelles remain in a liquid state [3]. When injected into a tumor, they stabilize into an *in situ* hydrogel depot through body heat triggered phase transition and β emission induced crosslinking [3]. This injectable brachytherapy source was then used to treat prostate and pancreatic tumor models in nude mice, resulting in >95% tumor regression in the prostate tumors and significant growth inhibition in the pancreatic tumors [3]. These results demonstrate promising advances in brachytherapy, but questions regarding dosimetry of the I-131 ELP remain. I-131 is used for radiation therapy primarily for its β emissions, with an average β energy of 182 keV [4]. Dose calculations using the absorbed fraction method for an average mouse tumor size and injection activity (see Table 2) result in an absorbed dose of $9.63 \times 10^3$ Gy (see section 2.1.1). Such an unreasonably high dose necessitates further scrutiny when considering the efficacy of treatment demonstrated by the mouse trials.

To better understand the dosimetry of the I-131 ELP and provide more feasible dose estimates, a simple model characterizing an average tumor treatment was
developed. It was hypothesized that due to the very short range of β particles in tissue and water, the I-131 ELP depot self-attenuated a significant portion of β emissions. This self-attenuation would then lead to a decrease in the dose to the tumor. Further, it was assumed that γ-emissions did not contribute to the absorbed dose as they were energetic enough to escape the bounds of the tumor. This model provided the basis to create a Monte Carlo simulation used to calculate absorbed dose and plot the dose distribution.

**Project 3**

The detection of β particles has often proven a troublesome task due to their relatively short range in solid materials [5]. This issue is exacerbated as the range of β particles approaches the thickness of conventional detector casings and entrance windows. This prohibits detection of β particles unless sufficiently thin entrance windows are used. Liquid scintillation assay techniques have been the preferred method to circumvent this issue, but such techniques are not applicable to all situations [5]. *In vivo* β detection is prohibited by conventional detector size and composition. Thermo- and optically stimulated luminescent dosimeters cannot function within a human, as exposing the phosphors to such an environment would destroy any readings. These restrictions limit our understanding of internal β dosimetry, as a lack of reliable detection requires that dose calculations be performed based on limited data and simulations.
A novel nano-fiber optic detector (nano-FOD) developed by Stanton et al. has been shown to produce a linear emissive response to x-ray radiation exposure [6]. The device is capable of functioning under many conditions that conventional detectors cannot, such as in vivo environments and direct contact with radiopharmaceuticals. If the nano-FOD can produce a similar response to β particles as it does x-rays, then it has promising applications as a novel form of β detector.
1. Project 1: Chest Phantom Development for Chest X-ray Radiation Protection Surveys

1.1 Materials and Methods

1.1.1 Acrylic Phantom Development

To develop a phantom that could accurately recreate the scatter radiation produced by a patient’s chest, tissue equivalent material matching the average adult’s chest wall thickness had to be used. Acrylic was chosen as it is a common tissue equivalent material used in many diagnostic imaging quality control applications [7]. The average adult chest wall thickness was found to be 4.08 cm at the 2nd intercostal space (ICS) midclavicular line and 4.55 cm at the 5th ICS anterior axillary line [8]. An industry standard acrylic sheet thickness of 3.81 cm was chosen to construct the phantom. This thickness was chosen to reduce the costs of materials and machining while remaining close to the desired anatomical thickness.

The 3.81 cm thick acrylic sheets were cut and assembled to form a 30.5 x 30.5 x 20.3 cm hollow box, as shown in Figure 1. The center of the acrylic phantom was left hollow to simulate the effects of air in the lungs. Six sheets of aluminum, each 1 mm thick, were cut to line the inside walls of the phantom to boost the scatter radiation if necessary. The aluminum sheets were cut in such a way as to allow for insertion or removal as needed.
1.1.2 Protocols and Measurements

The following three phantoms were used during the scatter survey:

1. CIRS ATOM® adult male phantom, model number 701-D

2. Acrylic phantom, with and without aluminum lining

3. 3 gallon water bottle

The thorax dimensions of the adult male phantom measured 30 x 32 x 23 cm. The dimensions of the water bottle measured 33 x 19 x 22 cm. The tissue and organ equivalent materials, sizes, and geometries of the adult male phantom are based on ICRP 23, ICRU 48, and other available anatomic reference data [9]. Therefore, it is assumed to accurately represent an adult human and considered the reference point for scatter radiation comparison.
The Philips digital radiography unit (model 9890 000 02-407) in Room 1511A2 of Duke Hospital North was used to conduct the scatter survey. A blue print of the room is included in Appendix A. Each phantom was setup and scanned according to posterior-anterior (PA) and lateral chest protocols as a normal adult patient would be, as shown in Figure 2. The source to bucky distance was 183 cm and automatic exposure control was used in each scan according to protocol. Two calibrated Victoreen 451P handheld pressurized μR ion chamber radiation survey meters were used to perform all measurements.
Figure 2: Setup for PA protocol (left column) and lateral protocol (right column). Phantoms include anthropomorphic (top row), acrylic (middle row, shown with aluminum lining), and 3 gallon water bottle.
Scatter radiation was measured at four points within the radiography room on the central plane of the detector panel. Each measurement location was 2 meters away from the center of the detector at four different angles depicted in Figure 3.

Figure 3: Angular distribution of measurement locations (depicted by red dots).

The two survey meters were set to cumulative mode for an exposure readout in μR. They were then held at 0° and 180° for five sets of measurements then held at 45° and 135° for another five sets of measurements. This process was repeated for each phantom and protocol. The measurements were then averaged and plotted as an angular distribution. Each angular distribution was grouped by protocol and distinguished by phantom type. Grouping the results by protocol allowed for easy comparison of the scatter radiation produced by each phantom. A polynomial trendline was added for each phantom to better distinguish the angular distributions. The percent difference (PD) of scatter radiation produced by the anthropomorphic phantom (A) and other phantoms (B) was calculated for each angle using equation 1.1.
\[ PD_{AB} = \left( \frac{A - B}{(A + B)/2} \right) \times 100 \] (1.1)

The percent difference values were then averaged for each phantom to determine which one best agreed with the anthropomorphic phantom.

Table 1 shows the average mAs and scan time for each phantom and protocol.

All scans were performed at 125 kVp using automatic exposure control.

Table 1: Average mAs and scan time for each phantom and protocol.

<table>
<thead>
<tr>
<th>Phantom Type</th>
<th>Protocol</th>
<th>mAs</th>
<th>Scan Time (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthropomorphic</td>
<td>PA</td>
<td>1.44</td>
<td>2.92</td>
</tr>
<tr>
<td></td>
<td>Lateral</td>
<td>7.71</td>
<td>15.40</td>
</tr>
<tr>
<td>Acrylic with Aluminum</td>
<td>PA</td>
<td>1.42</td>
<td>2.85</td>
</tr>
<tr>
<td></td>
<td>Lateral</td>
<td>0.91</td>
<td>1.83</td>
</tr>
<tr>
<td>Acrylic without Aluminum</td>
<td>PA</td>
<td>1.22</td>
<td>2.47</td>
</tr>
<tr>
<td></td>
<td>Lateral</td>
<td>1.06</td>
<td>2.15</td>
</tr>
<tr>
<td>3 Gallon Water Bottle</td>
<td>PA</td>
<td>5.01</td>
<td>10.07</td>
</tr>
<tr>
<td></td>
<td>Lateral</td>
<td>5.18</td>
<td>10.35</td>
</tr>
</tbody>
</table>

Tables containing the raw average exposure data for both protocols can be found in Appendix A.
1.2 Results and Discussion

1.2.1 PA Protocol Scatter Radiation Comparison

As shown in Figure 4, the water bottle produced significantly greater amounts of scatter radiation than the anthropomorphic phantom, with an average percent difference of 66.5 ± 42.0%. In the PA setup, the radiation beam must travel through 22 cm of water when scanning the water bottle. When scanning the anthropomorphic phantom, the beam travels through a greater amount of lung equivalent material than it does tissue equivalent material. This allows for a greater amount of scattering events to occur inside the water bottle than inside the anthropomorphic phantom, producing higher scatter measurements as a result. This effect is highly dependent on the angle as demonstrated.

Figure 4: PA protocol scatter radiation angular distribution.

As shown in Figure 4, the water bottle produced significantly greater amounts of scatter radiation than the anthropomorphic phantom, with an average percent difference of 66.5 ± 42.0%. In the PA setup, the radiation beam must travel through 22 cm of water when scanning the water bottle. When scanning the anthropomorphic phantom, the beam travels through a greater amount of lung equivalent material than it does tissue equivalent material. This allows for a greater amount of scattering events to occur inside the water bottle than inside the anthropomorphic phantom, producing higher scatter measurements as a result. This effect is highly dependent on the angle as demonstrated.
by the significantly increased amount of measured radiation produced by the water bottle at 45° and 135°.

Measurements taken at 135° were on average higher than those taken at 45°, which is somewhat unexpected due to symmetry. However, the measurements at these two angles were taken by different people with different heights. Therefore, the difference is likely the result of human error in handling the survey meters.

### 1.2.2 Lateral Protocol Scatter Radiation Comparison

![Figure 5: Lateral protocol scatter radiation angular distribution.](image)

As shown in Figure 5, none of the phantoms agreed with the anthropomorphic phantom when setup for a lateral protocol. The average percent difference in scatter
radiation between the anthropomorphic phantom and water bottle was $78.3 \pm 22.8\%$.

The average percent difference in scatter radiation between the anthropomorphic phantom and acrylic phantom with aluminum was $157.6 \pm 5.6\%$. Without the aluminum, the percent difference became $143.0 \pm 17.6\%$.

In the lateral protocol setup, the radiation beam travels through a greater amount of material in the anthropomorphic phantom than the other phantoms. The beam must travel 33 cm through the center of the anthropomorphic phantom, 30.5 cm through the acrylic phantom, and 22 cm through the water bottle. Additionally, there is a hollow recess containing the handle for the water bottle that further reduces the amount of material that the beam must travel through. This results in the anthropomorphic phantom producing higher readings at all angles. Because the center of the acrylic phantom is hollow, the radiation beam only travels through a cumulative 7.62 cm of acrylic along the central axis. While this is enough material to produce reasonable agreement with the anthropomorphic phantom in a PA setup, it is insufficient for a lateral setup.

### 1.2.3 Improving the Acrylic Phantom

The aluminum lining had very little effect on the amount of scatter radiation produced by the acrylic phantom. The average percent difference in measurements between the acrylic phantom with and without the aluminum was $7.7 \pm 6.1\%$. This is likely due to thinness of the sheets and how they interact with the beam. Rather than
producing significant scatter radiation, the aluminum sheets only hardened the beam. This caused a slight shift in mAs and scan time (as shown in Table 1) while producing little difference in scatter measurements.

To improve the agreement between the acrylic and anthropomorphic phantom, more material must be incorporated. The sheet thickness (3.81 cm) used in this project was chosen to reduce the cost of materials and machining while maintaining a comparable chest wall thickness to the midclavicular line (4.08 cm). For a thickness of 4.08 cm, the total chest wall path length would be 8.16 cm when traveling along the central axis. However, the total chest wall path length along the central axis of the acrylic phantom is 7.62 cm, resulting in a discrepancy of 0.54 cm. This discrepancy is relatively minor and is why the acrylic phantom was within 33% agreement of the anthropomorphic phantom during the PA protocol.

When considering a lateral protocol, the radiation beam must travel through a significantly larger path length of tissue before reaching the detector when compared to a PA protocol. The average chest wall thickness at the anterior axillary line was found to be 4.55 cm. When compared to the acrylic phantom, this results in a total chest wall path length discrepancy of 1.48 cm. This is nearly triple the amount of discrepancy found during a PA protocol, and likely accounts for the massive difference in agreement between the two protocols. By increasing the acrylic sheet thickness to better match
average chest wall dimensions, there would likely be a marked improvement in agreement between the acrylic and anthropomorphic phantom.
2. Project 2: Internal Beta Dosimetry of an Iodine-131 Labelled Elastin-Like Polypeptide

2.1 Materials and Methods

2.1.1 Assumptions and Approximations

Table 2 lists the variable definitions and values used to develop the I-131 ELP model. The injection dose, average tumor mass, volume of ELP depot, and effective half-life of the I-131 ELP were provided by Schaal et al. All other values were calculated based on assumptions and approximations about the geometry of the tumor. All calculations are shown below.

Table 2: Variable definitions and values for I-131 ELP model.

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$A_{dose}$</td>
<td>I-131 ELP injection dose</td>
<td>10 µCi/mg</td>
</tr>
<tr>
<td>$m_{tumor}$</td>
<td>Tumor mass</td>
<td>125 mg</td>
</tr>
<tr>
<td>$\rho_{tumor}$</td>
<td>Tumor density</td>
<td>1 g/cm$^3$</td>
</tr>
<tr>
<td>$A_0$</td>
<td>Initial activity of I-131 ELP depot</td>
<td>1.25 mCi</td>
</tr>
<tr>
<td>$T_{eff}$</td>
<td>Effective half-life of I-131 ELP</td>
<td>7.20 days</td>
</tr>
<tr>
<td>$V_{tumor}$</td>
<td>Volume of tumor</td>
<td>125 mm$^3$</td>
</tr>
<tr>
<td>$V_{ELP}$</td>
<td>Volume of ELP depot</td>
<td>41.7 mm$^3$</td>
</tr>
<tr>
<td>$r_{tumor}$</td>
<td>Radius of tumor</td>
<td>3.10 mm</td>
</tr>
<tr>
<td>$r_{ELP}$</td>
<td>Radius of ELP depot</td>
<td>2.15 mm</td>
</tr>
</tbody>
</table>

For a tumor mass and density of $m_{tumor} = 125$ mg and $\rho_{tumor} = 1$ g/cm$^3$, the tumor volume is

$$V_{tumor} = \frac{m_{tumor}}{\rho_{tumor}} = \frac{(0.125 \text{ g})}{(1 \text{ g/cm}^3)} = 125 \text{ mm}^3.$$
The tumor is approximated as a sphere, resulting in a radius of

\[ r_{tumor} = \left( \frac{3}{4\pi V_{tumor}} \right)^{1/3} = \left( \frac{3}{4\pi} (125 \text{ mm}^3) \right)^{1/3} = 3.10 \text{ mm}. \]

The ELP depot volume is approximately \( V_{ELP} = \frac{1}{3} V_{tumor} \), resulting in a volume and radius of

\[ V_{ELP} = \frac{1}{3} V_{tumor} = \frac{1}{3} (125 \text{ mm}^3) = 41.7 \text{ mm}^3 \]

\[ r_{ELP} = \left( \frac{3}{4\pi V_{ELP}} \right)^{1/3} = \left( \frac{3}{4\pi} (41.7 \text{ mm}^3) \right)^{1/3} = 2.15 \text{ mm}. \]

The initial activity of the I-131 ELP depot is a product of the tumor mass and injection dose.

\[ A_0 = m_{tumor} A_{dose} = (125 \text{ mg})(10 \mu\text{Ci/mg}) = 1.25 \text{ mCi} \]

The I-131 ELP is injected into the center of the tumor where it solidifies and forms a spherical depot. This displaces the mass of the tumor into a spherical shell surrounding the depot, as shown in Figure 6.

Figure 6: Spherical tumor with I-131 ELP depot.
Beta particles are emitted isotropically from within the I-131 ELP depot with an average energy of 182 keV (a decay scheme of I-131 can be found in Appendix B). Linear interpolation of NIST stopping powers for 182 keV electrons in tissue yields a total stopping power of 2.91 MeV/cm [10]. This leads to a range of 0.63 mm in tissue; therefore, it is assumed that all β emissions are confined within the bounds of the tumor. The average I-131 gamma emission energy is 382 keV [4]. Linear interpolation of NIST mass energy absorption coefficients for 382 keV photons in tissue yields an attenuation coefficient of 0.032 cm$^{-1}$ [11]. This leads to a mean free path of 31 cm; therefore, it is assumed that all γ emissions escape the tumor and do not contribute to the dose.

### 2.1.2 Absorbed Fraction Method Calculations

The absorbed fraction method allows for the calculation of absorbed dose delivered to a target organ from a source organ [5]. For the scenario depicted in Figure 6, the tumor is considered both the target and source organ. The steps to calculate the absorbed dose to the tumor are as follows:

1. Calculate the cumulated activity $\tilde{A}$ using equation 2.1
   \[ \tilde{A} = 1.44T_{eff}A_0 \]  
2. Determine the equilibrium absorbed dose constant $\Delta_i$ for each emission
3. Determine the absorbed fraction $\phi_i$ for each emission
4. Calculate the average absorbed dose using equation 2.2
   \[ \bar{D} = \frac{\tilde{A}}{m_{tumor}} \sum_i \phi_i \Delta_i \]
The cumulated activity of the I-131 ELP is

\[
\bar{A} = 1.44(7.20 \text{ days})(1.25 \text{ mCi}) = 3.11 \times 10^5 \mu\text{Ci} \cdot \text{h}.
\]

Table 3 includes the equilibrium absorbed dose constants for each I-131 \(\beta\) emission along with their sum [12].

**Table 3: Equilibrium absorbed dose constants for I-131 \(\beta\)-emissions.**

<table>
<thead>
<tr>
<th>Emission</th>
<th>(\Delta_i (\text{rad} \cdot \text{g/\muCi} \cdot \text{h}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\beta^- 1)</td>
<td>3.15E-03</td>
</tr>
<tr>
<td>(\beta^- 2)</td>
<td>1.15E-03</td>
</tr>
<tr>
<td>(\beta^- 3)</td>
<td>1.52E-02</td>
</tr>
<tr>
<td>(\beta^- 4)</td>
<td>3.65E-01</td>
</tr>
<tr>
<td>(\beta^- 6)</td>
<td>2.53E-03</td>
</tr>
<tr>
<td><strong>Total:</strong></td>
<td><strong>3.87E-01</strong></td>
</tr>
</tbody>
</table>

As determined in section 2.1.1, all \(\beta\) emissions are confined within the bounds of the tumor. Therefore, the absorbed fraction for each emission is \(\phi_i = 1\) and equation 2.2 becomes

\[
\bar{D} = \frac{\bar{A}\Delta}{m_{\text{tumor}}}.
\]  

(2.3)

Using equation 2.3, the absorbed dose to the tumor is

\[
\bar{D} = \frac{(3.11 \times 10^5 \mu\text{Ci} \cdot \text{h})(3.87 \times 10^{-1} \text{ rad} \cdot \text{g/\muCi} \cdot \text{h})}{(0.125 \text{ g})} = 9.63 \times 10^5 \text{ rad} = 9.63 \times 10^3 \text{ Gy}.
\]

Such an unreasonably large dose is a result of the limitations of the absorbed fraction method. The method implicitly assumes activity is distributed uniformly throughout an organ [5]. As shown in Figure 6, the activity is localized within the center of the tumor. Any dose to the tumor is the result of electrons radiating away from the I-131 ELP depot. This scenario results in the majority of \(\beta\) emissions being self-attenuated
by the ELP depot without ever reaching the tumor. Figure 7 depicts this behavior near the tumor-ELP boundary.

Figure 7: Closeup examination of the tumor-ELP boundary.

This behavior suggests that $\beta$ particles can only reach the tumor if they are emitted within 0.63 mm of the tumor-ELP boundary. However, particles that are emitted within the appropriate range also have the chance of being emitted inwards, resulting in ELP absorption. Under these conditions, the absorbed fraction method cannot provide an accurate dose calculation.
2.1.3 Monte Carlo Simulation

To better understand the dosimetry underlying the unique I-131 ELP scenario, a Monte Carlo simulation was performed. The Monte Carlo program FLUKA (a German acronym for FLUctuating KAscade) was chosen for this purpose as it allows for calculations of particle transport and interactions with matter [13]. The simulation was constructed based upon the model developed in section 2.1.1. A 3.10 mm radius sphere of soft tissue (ICRU Four-Component) was used to represent the tumor. A 2.15 mm radius sphere of water was placed inside the tumor to represent the I-131 ELP depot. A screenshot of the FLUKA geometry tab depicting this setup is shown in Figure 8.

![Figure 8: FLUKA screenshot of the tumor (tissue) and I-131 ELP depot (water) geometry.](image)

The 182 keV electrons were emitted isotropically from within the water sphere to simulate the I-131 ELP source within the tumor. Dose was scored for the water and
tissue regions separately to calculate the absorbed dose to the ELP depot and tumor, respectively. To generate a dose profile, dose was scored in 0.1 x 0.1 x 0.1 mm voxels along the x-axis. The voxel doses were normalized and plotted as a function of distance along the x-axis. The raw dose score output of FLUKA was in units of GeV/cm³/event.

This value was converted to units of Gy/event as follows

\[
[Dose] = \left( \frac{\text{GeV}}{\text{cm}^3} \times \frac{10^9 \text{ eV}}{\text{GeV}} \times \frac{1.6 \times 10^{-19} \text{ J}}{\text{eV}} \right) \left( \frac{1}{\text{event}} \times \frac{\rho_{\text{material}} (\text{g/cm}^3) \times \left( \frac{10^{-3} \text{ kg}}{\text{g}} \right) \times \left( \frac{10^3 \text{ kg}}{\text{g}} \right)}{\rho_{\text{material}} (\text{g/cm}^3) \times \left( \frac{10^{-3} \text{ kg}}{\text{g}} \right)} \right) = \left( \frac{1}{\text{kg}} \right) = \frac{\text{Gy}}{\text{event}}
\]

The absorbed dose was calculated by multiplying the dose output in Gy/event by the total number of events produced over the I-131 ELP’s lifetime. The total number of events was calculated from the cumulated activity of I-131.

\[
N_{\text{events}} = (3.11 \times 10^5 \mu\text{Ci} \cdot \text{h}) \times \left( \frac{10^{-6} \text{ Ci}}{\mu\text{Ci}} \right) \times \left( \frac{3.7 \times 10^{10} \text{ s}^{-1}}{\text{Ci}} \right) \times \left( \frac{3600 \text{ s}}{\text{h}} \right) = 4.14 \times 10^{13} \text{ events}
\]

The simulation was run multiple times at an increasing number of histories until reported values stabilized at 10⁹ histories.

### 2.2 Results and Discussion

Table 4 lists the FLUKA dose output for both regions along with the calculated absorbed dose.

<table>
<thead>
<tr>
<th>Region</th>
<th>FLUKA Output (Gy/event)</th>
<th>Absorbed Dose (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor</td>
<td>1.75 × 10⁻¹²</td>
<td>7.23 × 10¹</td>
</tr>
</tbody>
</table>
For an injected activity of 1.25 mCi, the tumor receives an absorbed dose of 72.3 Gy. Common monotherapy prescription doses for prostate brachytherapy are 145 and 125 Gy for I-125 and Pd-103, respectively [14]. This would suggest that the values obtained from the simulation correlate to realistic treatment plans. As hypothesized, the ELP depot self-attenuates the majority of $\beta$ emissions, resulting in an absorbed dose of $1.14 \times 10^3$ Gy to the ELP. This confirms that conventional dose calculation methods such as the absorbed fraction method cannot be applied to the unique ELP treatment geometry.

Figure 9 depicts the normalized dose profile along the x-axis of the tumor and ELP depot, with the boundary between the two regions demarked by dashed lines. Approximately, 99% of the absorbed dose to the tumor is highly localized to a 0.3 mm region surrounding the ELP depot. This achieves the desired effect of treating the tumor while sparing surrounding normal tissue, as demonstrated by the mouse trials [3].
Figure 9: Dose profile of the tumor and I-131 ELP depot. Black lines demark the tumor-ELP boundary and red lines demark the periphery of the tumor.

Such extreme dose localization raises questions as to how the entire tumor is treated. The model used to calculate absorbed dose does not consider diffusion of the ELP throughout the tumor. Rather, it assumes that the ELP solidifies instantaneously when injected – forming an abrupt junction within the tumor. However, once injected, the ELP has been shown to take approximately 2 minutes to solidify due to thermal stabilization [3]. During the brief interval where the ELP remains a liquid, it is believed that there is a small degree of diffusion throughout the tumor. As the ELP diffuses and solidifies, it would form a concentration gradient throughout the tumor rather than an abrupt junction. Another possibility is that the tumor shrinks around the ELP as the region receiving dose is killed. These mechanisms would allow for dose delivery to the outer regions of the tumor and account for the >95% prostate cancer regression.
However, the pharmacokinetics of the ELP needs further investigation before any conclusions regarding concentration distributions can be drawn.
3. Project 3: I-131 Beta Detection Using a Scintillating Nanoparticle Detector

3.1 Nano-FOD Overview

The nano-FOD functions via measuring light emissions from scintillating Eu- and Li-doped yttrium oxide nanocrystals optically glued to the tip of a fiber optic cable. When exposed to ionizing radiation, the crystals emit a spectrum of light peaking between the 605 – 617 nm wavelength domain [6]. These light emissions are collected by the optical fiber and recorded using a CCD-photodetector. When integrated over the 605 – 617 nm wavelength domain, a voltage signal is obtained that can be correlated to radiation exposure. Through this correlation, the nano-FOD is calibrated to function as a real-time radiation detector. Findings thus far have demonstrated a linear correlation between incident radiation dose and nano-FOD signal output [6]. There is no evidence of scintillation intensity saturation at the highest energies measured to date, allowing for nano-FOD applications at diagnostic imaging (80 kVp) and radiation therapy (6 MV) energy levels [6].

Applications of the nano-FOD to β detection have not previously been explored. Therefore, to determine if a measurable response could be produced, the nano-FOD was placed in direct contact with the radioisotope I-131 – a common β emitter used in various thyroid treatments [5]. The response was measured as the I-131 decayed over 17 days to determine the activity dependence of the signal and establish any possible correlations.
3.2 Materials and Methods

3.2.1 I-131 and Nano-FOD Setup

I-131 is a readily available radioisotope that primarily emits $\beta$ particles with an average energy of 182 keV [4]. For this reason, it was chosen to test the nano-FOD’s $\beta$ response. A 15 mL glass screw top vial was used to contain the I-131 and was placed inside an approximately 3 cm thick lead pig for shielding. The vial contained an initial concentration of 101 mCi of I-131 in 2 mL of stabilizing solution. The stabilizing solution was comprised of 0.05% Sodium Metabisulfite, 0.2% Disodium EDTA, and 0.5% Sodium Phosphate (Dibasic and Anhydrous). To allow the sensitive volume of the nano-FOD tip to come in direct contact with the I-131, a 1 mm diameter hole was drilled through the tops of both the glass vial and lead pig. The holes were aligned to allow the nano-FOD to be inserted into the vial and submerged in the I-131, as shown in Figure 10.

![Figure 10: Nano-FOD inserted into the vial and submerged in I-131. The right image depicts the cable highlighted in red.](image)
The lead pig was placed behind an L-block for further shielding. To perform measurements, the nano-FOD cable was attached to the CCD-photodetector. The analog voltage signal produced by the photodetector was then sent to a data acquisition (DAQ) board connected to a laptop. A LabVIEW program would then display and record the signal in real-time. Figure 11 depicts this setup.

![Diagram of nano-FOD setup](image)

**Figure 11: Diagrammatic depiction of the nano-FOD setup.**

### 3.2.2 Measurements and Calculations

Each day over a 17 day period, a set of 5 measurements was acquired. The time and date at the beginning of data acquisition was recorded for each set. To acquire a single measurement, the nano-FOD tip was fully submerged in the I-131 for approximately 10 seconds. It was then completely withdrawn from the I-131 for approximately 10 seconds. This process was repeated until a complete set of 5 measurements was recorded. Figure 12 depicts the change in signal as the nano-FOD interacted with the I-131.
The activity remaining on the nano-FOD tip after being withdrawn from the I-131 was measured with a survey meter and found to be in the sub microcurie range. There was no discernable signal at this level of activity, therefore, the signal obtained when withdrawn from the I-131 was considered background.

To establish correlations between the nano-FOD signal and radiation exposure, the net signal must be calculated. The net signal is the difference between the signal obtained when the nano-FOD is exposed to radiation minus the background signal when it is not exposed. Figure 13 depicts a sample set of measurements defining the signal and background.
The net signal was calculated using equation 3.1.

\[ Net \text{ Signal} = Signal - Background \]  

(3.1)

The signal-to-noise ratio was calculated using equation 3.2, where \( \sigma_{\text{Signal}} \) was the standard deviation of the signal.

\[ SNR = \frac{Net \text{ Signal}}{\sigma_{\text{Signal}}} \]  

(3.2)

The activity of I-131 was calculated for each set of measurements based on the time and date of acquisition using equation 3.3.

\[ A = A_0 \exp \left( -\frac{\ln(2) \Delta t}{T_{1/2}} \right) \]  

(3.3)

Where \( A_0 \) was the activity during the previous acquisition, \( \Delta t \) was the time elapsed since the previous acquisition, and \( T_{1/2} \) was the half-life of I-131 (8.02 days). Both the net signal and SNR were plotted as functions of the concentration of I-131 in mCi/mL.
3.3 Results and Discussion

As shown in Figure 12, the nano-FOD produced a measurable signal when exposed to the I-131. Approximately 90% of local irradiation by I-131 is the result of $\beta$ emissions while the remaining 10% is the result of $\gamma$ emissions [15]. Therefore, it is reasonable to believe that the signal produced by the nano-FOD was primarily the result of exposure to $\beta$ emissions.

![Figure 14: Nano-FOD net signal response as a function of I-131 concentration.](image)

As shown in Figure 14, there was a linear correlation between the net signal and I-131 concentration. Extrapolation of the trendline suggests that signal cutoff would occur at a concentration of 6.1 mCi/mL. In Project 2, the standard concentration of I-131...
used for ELP brachytherapy was 10 mCi/mL. For such a scenario, the nano-FOD could be utilized as a real-time, *in vivo* detector.

![Figure 15: Nano-FOD signal-to-noise ratio as a function of I-131 concentration.](image)

As shown in Figure 15, there was a linear correlation between the SNR and I-131 concentration. Extrapolation of the trendline suggests that the SNR would equal 1 at a concentration of 11.7 mCi/mL. Therefore, the SNR would drop below 1 before signal cutoff occurred.
Conclusions

Project 1

For the PA protocol – both with and without the aluminum lining – the acrylic phantom performed far more favorably than the water bottle. With the aluminum lining, the average percent difference between the acrylic and anthropomorphic phantom was 33.3 ± 28.8%. Without the aluminum lining, the percent difference became 33.0 ± 21.2%. This would suggest that the acrylic phantom serves as a more accurate representation of an average adult’s chest than the water bottle. However, such results depend highly on the protocol and angle of measurement, as demonstrated by the lateral protocol results.

Project 2

The current model has provided a valuable foundation for understanding the dosimetry underlying the I-131 ELP brachytherapy technique developed by Schaal et al. Results have demonstrated that the I-131 ELP delivers doses that are comparable to those of traditional brachy monotherapy techniques. Several avenues for refinement of the model include:

1. Implementation of the ELP micelle compound into the material database
2. More information regarding the pharmacokinetics of the ELP
3. Implementation of an ELP concentration gradient throughout the tumor
4. Realistic tumor geometries
Implementation of such refinements would provide a model capable of reliable and invaluable assistance in further developing this unique ELP brachytherapy method.

**Project 3**

Results have shown that the nano-FOD produces a measurable signal when exposed to the β emissions of I-131. These results have demonstrated the possibility of applying nano-FOD technology to real-time β detection. The next milestone would be developing a method to correlate signal to exposure. As discussed in the introduction, there are few conventional detection methods available for such a task. Therefore, the most likely approach to calibrating the nano-FOD would be through Monte Carlo simulations. Implementing the same experimental setup used here into a simulation could provide the exposure readings necessary to develop a calibration curve.
Figure A1: Floor plan of room 1511A2.
Table A1: PA protocol exposure data.

<table>
<thead>
<tr>
<th>Anthromorphic Phantom</th>
<th>Angle (degrees)</th>
<th>0</th>
<th>45</th>
<th>135</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Exposure (µR)</td>
<td>3.81</td>
<td>6.27</td>
<td>6.53</td>
<td>2.77</td>
<td></td>
</tr>
<tr>
<td>Standard Deviation (µR)</td>
<td>2.08</td>
<td>2.61</td>
<td>2.22</td>
<td>1.15</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acrylic Phantom With Aluminum</th>
<th>Angle (degrees)</th>
<th>0</th>
<th>45</th>
<th>135</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Exposure (µR)</td>
<td>2.02</td>
<td>3.58</td>
<td>5.94</td>
<td>2.57</td>
<td></td>
</tr>
<tr>
<td>Standard Deviation (µR)</td>
<td>1.31</td>
<td>0.45</td>
<td>1.40</td>
<td>1.34</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Acrylic Phantom Without Aluminum</th>
<th>Angle (degrees)</th>
<th>0</th>
<th>45</th>
<th>135</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Exposure (µR)</td>
<td>2.24</td>
<td>3.81</td>
<td>5.15</td>
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<td></td>
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<tr>
<td>Standard Deviation (µR)</td>
<td>1.74</td>
<td>1.68</td>
<td>1.45</td>
<td>1.34</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3 Gallon Water Bottle Phantom</th>
<th>Angle (degrees)</th>
<th>0</th>
<th>45</th>
<th>135</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Exposure (µR)</td>
<td>4.48</td>
<td>13.22</td>
<td>25.54</td>
<td>5.15</td>
<td></td>
</tr>
<tr>
<td>Standard Deviation (µR)</td>
<td>0.00</td>
<td>2.59</td>
<td>3.88</td>
<td>0.74</td>
<td></td>
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</tbody>
</table>

Table A2: Lateral protocol exposure data.

<table>
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<th>Anthromorphic Phantom</th>
<th>Angle (degrees)</th>
<th>0</th>
<th>45</th>
<th>135</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Exposure (µR)</td>
<td>10.53</td>
<td>29.79</td>
<td>34.65</td>
<td>14.26</td>
<td></td>
</tr>
<tr>
<td>Standard Deviation (µR)</td>
<td>1.14</td>
<td>11.43</td>
<td>6.48</td>
<td>3.17</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acrylic Phantom With Aluminum</th>
<th>Angle (degrees)</th>
<th>0</th>
<th>45</th>
<th>135</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Exposure (µR)</td>
<td>1.34</td>
<td>3.14</td>
<td>3.56</td>
<td>1.98</td>
<td></td>
</tr>
<tr>
<td>Standard Deviation (µR)</td>
<td>0.45</td>
<td>1.93</td>
<td>0.79</td>
<td>1.08</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acrylic Phantom Without Aluminum</th>
<th>Angle (degrees)</th>
<th>0</th>
<th>45</th>
<th>135</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Exposure (µR)</td>
<td>2.69</td>
<td>4.70</td>
<td>3.76</td>
<td>2.18</td>
<td></td>
</tr>
<tr>
<td>Standard Deviation (µR)</td>
<td>1.95</td>
<td>3.28</td>
<td>0.40</td>
<td>0.74</td>
<td></td>
</tr>
<tr>
<td>Angle (degrees)</td>
<td>0</td>
<td>45</td>
<td>135</td>
<td>180</td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>Average Exposure (µR)</td>
<td>5.35</td>
<td>8.35</td>
<td>16.80</td>
<td>7.17</td>
<td></td>
</tr>
<tr>
<td>Standard Deviation (µR)</td>
<td>1.66</td>
<td>0.80</td>
<td>8.26</td>
<td>2.61</td>
<td></td>
</tr>
</tbody>
</table>
### Appendix B

Table B1: I-131 decay scheme [12].

**53-iodine-131**

**Half-life** = 8.04 days

**Decay mode(s):** $\beta^-$

<table>
<thead>
<tr>
<th>Radiation</th>
<th>Particles/Transition</th>
<th>Energy/Particle $E(i)$ (MeV)</th>
<th>Energy/transition $\Delta(i)$ rad/$\mu$Ci/h Gy/kg/Bq/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta^-$ 1</td>
<td>2.13E-02</td>
<td>6.935E-02†</td>
<td>3.15E-03</td>
</tr>
<tr>
<td>$\beta^-$ 2</td>
<td>6.20E-03</td>
<td>8.693E-02†</td>
<td>1.15E-03</td>
</tr>
<tr>
<td>$\beta^-$ 3</td>
<td>7.36E-02</td>
<td>9.660E-02†</td>
<td>1.52E-02</td>
</tr>
<tr>
<td>$\beta^-$ 4</td>
<td>8.94E-01</td>
<td>1.915E-01†</td>
<td>3.65E-01</td>
</tr>
<tr>
<td>$\beta^-$ 6</td>
<td>4.20E-03</td>
<td>2.832E-01†</td>
<td>2.53E-03</td>
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<tr>
<td>y 1</td>
<td>2.62E-02</td>
<td>8.018E-02</td>
<td>4.48E-03</td>
</tr>
<tr>
<td>ce-K, y 1</td>
<td>3.63E-02</td>
<td>4.562E-02</td>
<td>3.53E-03</td>
</tr>
<tr>
<td>ce-L1, y 1</td>
<td>4.30E-03</td>
<td>7.473E-02</td>
<td>6.85E-04</td>
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<tr>
<td>y 4</td>
<td>2.65E-03</td>
<td>1.772E-01</td>
<td>1.00E-03</td>
</tr>
<tr>
<td>y 7</td>
<td>6.06E-02</td>
<td>2.843E-01</td>
<td>3.67E-02</td>
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<tr>
<td>ce-K, y 7</td>
<td>2.48E-03</td>
<td>2.497E-01</td>
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<tr>
<td>y 12</td>
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<td>3.258E-01</td>
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<td>y 14</td>
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<td>3.299E-01</td>
<td>1.09E-02</td>
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<tr>
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<td>3.590E-01</td>
<td>1.31E-03</td>
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<td>y 16</td>
<td>3.61E-03</td>
<td>5.030E-01</td>
<td>3.87E-03</td>
</tr>
<tr>
<td>y 17</td>
<td>7.27E-02</td>
<td>6.370E-01</td>
<td>9.87E-02</td>
</tr>
<tr>
<td>y 18</td>
<td>2.20E-02</td>
<td>6.427E-01</td>
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</tr>
<tr>
<td>y 19</td>
<td>1.80E-02</td>
<td>7.229E-01</td>
<td>2.77E-02</td>
</tr>
<tr>
<td>Kα₁, x-ray</td>
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<td>2.978E-02</td>
<td>1.64E-03</td>
</tr>
<tr>
<td>Kα₂, x-ray</td>
<td>1.40E-02</td>
<td>2.946E-02</td>
<td>8.79E-04</td>
</tr>
</tbody>
</table>

Listed $x, y$ and $y^\pm$ radiations $8.10E-01$ $6.09E-14$

Omitted $x, y$ and $y^\pm$ radiations† $2.32E-03$ $1.75E-16$

Listed $\beta, ce$ and Auger radiations $4.05E-01$ $3.04E-14$

Omitted $\beta, ce$ and Auger radiations† $3.96E-03$ $2.98E-16$

Listed radiations $1.21E+00$ $9.13E-14$

Omitted radiations‡ $6.29E-03$ $4.73E-16$

† Average energy

‡ Each omitted transition contributes <0.100% to $\Sigma \Delta(i)$ in its category.

XENON-131M daughter, yield 1.11E-02, is radioactive.

XENON-131 daughter, yield 9.889E-01, is stable.
References


