I, Jason L. Collier, hereby submit this original work as part of the requirements for the degree of Master of Science in Mechanical Engineering.

It is entitled:
Uptake and exposure measurements in Health Physics Technicians associated with 131I-MIBG patient therapy

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Uptake and exposure measurements in Health Physics Technicians associated with $^{131}$I-MIBG patient therapy

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Graduate School
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Abstract

$^{131}$I-metaiodobenzylguanidine, $^{131}$I-MIBG, has increasingly been used as an effective radiotherapeutic agent for pediatric patients diagnosed with neuroblastoma. While not a cure, the agent allows patients the possibility of controlling their disease and lengthening disease stabilization. Radioiodine pharmaceuticals were reformulated in 1979 to reduce exposure to those attending to the patient by reducing the volatility of the iodine and increasing the use of encapsulation to limit the quantity of unbound radioiodine. However, therapeutic $^{131}$I-MIBG may still be administered to the patient through a liquid form. Health physics technicians are responsible for ensuring regulatory compliance and safety in and around the patient’s room. This study was performed to determine if the health physics technicians were exposed to $^{131}$I while performing required tasks within the patient’s treatment room. Results showed that per therapeutic treatment, the health physics technicians were exposed to an average of $6.9 \times 10^{-1} \mu$Sv hr$^{-1}$ GBq$^{-1}$. Furthermore, trace contaminate levels of $^{131}$I were detected by direct, in vivo measurement in persons having a normal and hypoactive thyroid. In vivo measurements were performed using a single 2900 mm$^2$ high resolution germanium detector positioned approximately 3 cm from the thyroid while the subject was seated in a shielded room. The thyroid activity measured in the technicians was well below requirements for monitoring established by the U.S. Nuclear Regulatory Commission. Established methods and working conditions are adequate to insure that radiation exposure to health physics technicians supporting the $^{131}$I-MIBG radioiodine therapeutic procedures are consistent with the program to keep exposure as low as reasonably achievable.
Acknowledgements

First and foremost, I’d like to thank my wife, Andrea, for her immense amount of patience and encouragement in completing my master’s degree. I would like to thank Dr. Henry Spitz for all of his mentoring and enthusiasm in health physics. I’d also like to thank Dramane Konate for his assistance and guidance in the pursuit of completing my thesis. Lastly, I’d like to thank the University of Cincinnati’s Radiation Safety Office for their time and energy in completing my research.
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INTRODUCTION
Neuroblastoma is the most common extracranial solid tumor seen in pediatric patients, occurring anywhere sympathetic nervous tissue is present. A malignant tumor arising from primordial cells, neuroblastoma affects approximately 6.46 per 100,000 infants and represents 28% of all infant malignancies (Ries 1999). There are approximately 650 cases per year in the United States with patients under the age of two years accounting for nearly half of all documented cases (Scarsbrook 2007). $^{131}$I-metaiodobenzylguanidine ($^{131}$I-MIBG) has increasingly been administered more commonly as a therapeutic procedure for pediatric neuroblastoma patients. MIBG is a norepinephrine analog which concentrates in adrenergic tissue. It is believed that the MIBG is taken up into the sympathetic neuroeffector cells by a specific catecholamine type I active uptake mechanism and thereby stored in adrenergic storage vesicles (McEwan 1985).

Unbound radioiodine is inherently volatile and was reformulated in 1979 due to high occupational ionizing radiation exposures (Nishiyama 1980). Pharmaceutical radioiodine has frequently been kept in encapsulation to further limit potential contamination exposures to occupational workers. Unlike conventional capsule delivery in diagnostic MIBG procedures, therapeutic $^{131}$I-MIBG procedures may be delivered through a liquid solution. The expected amount of volatile $^{131}$I released from a capsule is approximately 0.001% of the therapeutic dose activity (Bright 2000). There remains a significant risk of contamination and uptake intrinsic with a liquid $^{131}$I solution. If exposed to the skin, absorption of iodine within a liquid solution ranges from 0.06 – 0.19% of the exposed activity (Muikku 2014) and the estimated absorbed $^{131}$I-MIBG dose to the thyroid is $8.9 \times 10^{-2}$ mGy MBq$^{-1}$ (Jabobsson 1986).

BACKGROUND
A Health Physics Technician (HPT) performs multiple auxiliary tasks associated with the $^{131}$I-MIBG treatment of patients that are designed to minimize exposure to health practitioners, family members,
and ancillary workers. The HPT is required by regulations to perform radiation measurements in and around the patient’s treatment room and they are also responsible for decontaminating facilities and recovering contaminated materials soiled by the patient during and after treatment. The sources of exposure may be aerosolization of material exhaled by the patient, resuspension of surface contaminants during post treatment area decontamination, or physical contact with surface contamination.

The HPT is trained in work procedures to ensure that little or no radiation exposure is received during the support of a $^{131}$I-MIBG patient treatment. These work procedures were developed so that any exposure received by the HPT is as low as reasonably achievable (ALARA), a practice in Health Physics in which methods and training programs are implemented to insure that any risk associated to radiation exposure is balanced by the benefits to the worker and patient.

**RESEARCH OBJECTIVE**
The primary objective of this study is to determine potential uptake and exposure of $^{131}$I by performing direct, in vivo measurements of $^{131}$I in the thyroid of health physics technicians who have completed a work assignment with a $^{131}$I-MIBG patient treatment.

**RADIATION RISK**
HPTs may receive some low level radiation exposure as they fulfill routine responsibilities of their position. The ALARA program has evaluated the risks associated with work place radiation exposures that may be received in the course of fulfilling routine job responsibilities. Fortunately, risk of health effects associated with low levels of occupational exposure (i.e., below 100 mSv) are unlikely according to the position statement of the Health Physics Society (HPS 2010).
Historically, the primary environmental sources of $^{131}$I were associated with atmospheric weapons testing, the large accident that occurred in the Ukraine at the Chernobyl nuclear power plant, and the recent tsunami that destroyed several nuclear power plants at Fukushima, Japan. In comparison, commercial nuclear power plants release very little $^{131}$I. The radioisotope is produced during uranium or plutonium fission with an approximate yield of 1.5 – 2.0% (ATSDR 2002). Nuclear medicine departments at most hospitals use large quantities of $^{131}$I in the form of radiopharmaceuticals for diagnosis and treatment of disease. Radiation emitted during decay of $^{131}$I includes both beta particles and photons with a radiological half-life of 8.03 days.

Due to the similarities of $^{131}$I-MIBG to norepinephrine, after infusion there is localization in normal tissues with extensive sympathetic innervation and tissues involved in metabolism and excretion (Nakajo 1983). The critical organs for $^{131}$I-MIBG are the bladder wall and liver for an average adult (70 kg) with an estimated organ dose of $8.1 \times 10^{-1}$ mGy MBq$^{-1}$. Furthermore, the estimated thyroid dose is $8.9 \times 10^{-2}$ mGy MBq$^{-1}$ for an average adult (Jabobsson 1986). For non-diseased adults, 55% of $^{131}$I-MIBG is excreted unchanged in the urine within 24 hours and 90% in four days (Mangner 1986). Primarily attributed to its guanidine side chain, $^{131}$I-MIBG is considered very stable in vivo with little metabolism resulting in a release of 2 – 6% unbound iodine (Kowalsky 2004). The effective half-life of $^{131}$I-MIBG is directly proportional to the disease extent within the patient.

Prior to infusion, the nuclear medicine technologist performs quality assurance of the $^{131}$I-MIBG therapy dose to ensure that $\geq 95\%$ of the $^{131}$I is bound to the MIBG pharmaceutical. Approximately 30% of the unbound radioiodine entering the blood system is taken up by the thyroid with the remaining excreted in urine (ICRP 1997). The average daily intake of iodine is approximately 300 $\mu$g however; the distribution and uptake is highly variable and very dependent on the individual, dietary intake, and thyroid function (Kowalsky 2004). A 25% uptake in the thyroid of unbound $^{131}$I would result in an
approximate dose of $3.6 \times 10^2$ mGy MBq$^{-1}$ for an average euthyroid adult, and a dose of $4.6 \times 10^1$ mGy MBq$^{-1}$ and $3.5 \times 10^2$ mGy MBq$^{-1}$ to the bladder wall and liver respectively (Sodium 2015). Due to the critical organ of $^{131}$I being the thyroid and the greater dose to the thyroid in comparison to $^{131}$I-MIBG, it is assumed the risk to non-diseased individuals is primarily proportional to the unbound $^{131}$I inhaled. The effective half-life of $^{131}$I is driven primarily by its short physical half-life (Muikku 2014).

The most significant health risks associated with exposure to unbound $^{131}$I involve the thyroid gland largely due to the sodium iodide symporter within the thyroid itself increasing the radioiodine uptake (Dohan 2003). An increase of cancer incidence has been shown in cohort studies among irradiated individuals, especially children. The 1986 Chernobyl accident demonstrates that children experience an increase in cancer rate (Institute 1999).

Current radiation safety standards and practices are based on the linear dose-response model, which implies a small risk is associated with each increment in exposure. The low dose risk is a conservative assumption that is convenient for developing radiation safety regulations. However, there is a lack of information to support or disprove low dose exposure effects. It is assumed that radiation exposure is directly proportional to the deterministic effects they cause. These assumptions are the basis for the dose-response relationship commonly referred to as the “linear-no-threshold” model. The National Academy of Science claims that current scientific evidence is consistent with the linear-no-threshold model (BEIR VII 2006). It is important to stress that no radiogenic health effects have been related to doses below 100 mSv (HPS 2010). The Health Physics Society suggests that quantitative risk assessments be established for doses greater than 50 mSv per year or 100 mSv over a lifetime and that only credible scientific evidence and its uncertainties be considered in evaluating dose as it relates to radiogenic health effects. (HPS 2010; HPS 2013).
MATERIALS AND METHODS
The clinical protocol for patient therapy using $^{131}$I-MIBG permits administration of up to 37 GBq of $^{131}$I-MIBG by intravenous infusion. The patient remains in a hospital room for approximately 3 - 5 days until the dose rate measured at a distance of one meter away from the source of highest exposure falls below 0.07 mSv/hr (U.S. NRC 1997). The HPT is responsible for performing daily radiation exposure surveys in and around the patient’s room, decontamination and collection of patient’s soiled materials, and decontamination of the hospital room after the patient has been released.

Exposure evaluations were performed for 4 different male HPTs who supported 5 different $^{131}$I-MIBG patient treatment procedures over a span of 14 months. Direct, in vivo thyroid measurements were performed for each HPT after they completed their respective tasks. Any in vivo measurements results from the thyroid were assumed directly from the unbound $^{131}$I the HPT may have been exposed to. One of the HPTs (HPT-A) has been clinically diagnosed with hypothyroidism disease.

HPTs were monitored for radiation exposure or contamination using three different methods. Method 1, external dose, involved wearing a personal electronic pocket dosimeter (PDM) near their thyroid to determine external exposure received directly from the patient and/or contaminants. The PDM was a RADOS RAD-60R (Figure 1), which uses an energy compensated silicone diode detector for measuring photons and x-rays. These dosimeters are calibrated on an annual basis.

Method two, thyroid deposition, involves performing a routine thyroid measurement for $^{131}$I using a collimated 2 inch x 2 inch NaI(Tl) detector with a Canberra Osprey digital MCA (Figure 2) between 6 hours and 3 days after the last potential uptake. The time of the measurement depended upon the work schedule for the HPT. Routine measurements consisted of 10 minutes in length with the detector located approximately 18 cm from the thyroid. Background measurements are performed for 10 minutes with the detector located over the thigh.
Method three, thyroid deposition WB, involves performing a thyroid measurement at the University of Cincinnati In Vivo Measurement Laboratory. This laboratory has an array of Canberra Model GL2820RS 2900 mm² high resolution germanium detectors installed in a 2.44 m² steel shielded room (Figure 3). Each HPT is measured for 30 – 60 minutes using one detector positioned approximately 3 cm from the thyroid (Figure 4) within 48 hours after the last exposure to the patient or upon completion of the decontamination of the treatment room. The Canberra Genie2K Gamma Acquisition and Analysis Software were used to collect and analyze thyroid measurements for methods 2 & 3. Both of the thyroid measurement systems successfully participate in the Thyroid Radioiodine Intercomparison Program (TRIP) conducted semiannually by Lawrence Livermore National Laboratory using standards containing precisely known quantities of $^{131}$I NaI (100 mg mL$^{-1}$) and sodium thiosulfate (200 mg mL$^{-1}$).

Treatments typically require isolation and hospitalization of the patient for a period of 3-5 days. Treatments are infrequent and in most cases, only one HPT is assigned to each patient treatment procedure. However, work schedules can be modified to accommodate vacations and holidays. No unforeseen issues or difficulties were developed during the observed treatment processes.

**RESULTS**

Tables 1 and 2 list the $^{131}$I treatment doses and monitoring results for each HPT.

**Method 1: External Dose**

The health physics technicians received a total external dose ranging from 6 $\mu$Sv to 42 $\mu$Sv as measured by personal electronic dosimeters. The times for patient isolation for the observed treatments were 4 to 5 days. The duration of time the assigned HPT was in the patient room is listed on Table 1 along with the measured thyroid deposition and external dose. The average external dose received by an HPT per unit $^{131}$I-MIBG infused was $6.9 \times 10^{-1}$ $\mu$Sv hr$^{-1}$ GBq$^{-1}$. 

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**Method 2: Thyroid Deposition**

Each HPT was monitored for $^{131}$I in the thyroid within 6 hours to 3 days post exposure by performing a 10 minute measurement using a 2 inch x 2 inch collimated NaI(Tl) detector. The minimum detectable activity (MDA) for the measurement was 148 Bq. No results exceeded the MDA.

**Method 3 Thyroid Deposition WBC**

Each HPT was measured within 48 hours after exposure at the University of Cincinnati In Vivo Measurement Lab. Each measurement was 30 to 60 minutes in length and was based upon the intensity of the 0.364 MeV energy peak (Figure 5). Table 2 lists the thyroid monitoring results for each HPT. The highest detectable activity occurred in treatment 2 with a measured $20.1 \pm 1.30$ Bq in the thyroid region and lowest activity was measured in treatment 4 with $0.08 \pm 0.05$ Bq in the thyroid region, equivalent to MDA. The calculated thyroid intake from treatment 2 resulted in $134.9$ Bq after decay correction. All thyroid intakes were assumed from the unbound $^{131}$I that the HPT may have been exposed to.

**DISCUSSION**

The most significant potential source of radiation exposure to the HPT occurs immediately after infusion of the $^{131}$I-MIBG liquid solution due to the high concentrated activity, the volatility of the liquid solution, and the inhalation potential from aerosolized contaminants in the patient’s breath. Other risks associated with the procedure come from handling and decontaminating soiled materials along with decontaminating the room after the patient release. The Nuclear Regulatory Commission (NRC) requires monitoring of workers who may receive more than 10% of the annual occupational limit. The annual limit on intake (ALI) is defined by the NRC as the amount of radioisotope inhaled or ingested by a worker in a year that would result in a committed effective dose equivalent of 50 mSv, or a committed effective equivalent dose to an individual organ or tissue of 500 mSv. The ALI for $^{131}$I is 1.85 MBq and is equivalent to average air concentration for $^{131}$I at $7.7 \times 10^{-4}$ Bq/mL. The quarterly monitoring
requirement for $^{131}$I uptake is $4.62 \times 10^{-2}$ MBq (U.S. NRC 2006). Regulations require an investigation when 2% intake of the ALI is measured through bioassay analysis for $^{131}$I.

The average dose rate for the HPTs was $6.9 \times 10^{-1}$ $\mu$Sv hr$^{-1}$ GBq$^{-1}$ recorded by the electronic personal dosimeter. Although none of the results from the routine monitoring with the collimated NaI(Tl) detector exceeded the MDA, trace quantities of $^{131}$I were recorded for all subjects using the whole body counter. None-the-less, all the results for the HPTs were well below NRC monitoring limits with an intake range of 0.3 – 134.9 Bq. Intake values were calculated with respect to ICRP 30/NUREG CR-4884 (NUREG 1988). No intake was calculated for HPT-A as they have been clinically diagnosed with hypothyroidism. Required investigational levels for thyroid uptake begin at $3.7 \times 10^{4}$ Bq.

Evidence from treatment 5 indicates that the highest potential uptake of $^{131}$I by an HPT occurs during the decontamination phase of the HPT’s tasks. The lowest thyroid deposition was measured in HPT-D whose primary tasks were conducted prior to the patient release and room decontamination. HPT-C, who performed the decontamination tasks during treatment 5 of the patient’s room post release, had detectable activity similar to that of the other treatments. This could be attributed to the resuspension of the $^{131}$I contaminants during the removing of protective coverings within the patient’s room.

Nuclear medicine technologists handle the $^{131}$I-MIBG vial and administer the infusion of the liquid solution to the patient. On average, they receive an exposure of $0.024$ $\mu$Sv MBq$^{-1}$ for doses ranging from 9.25 – 31.1 GBq putting them at a higher risk in comparison to the HPT, but still well below NRC exposure monitoring limits (Turpin 2013).

HPTs are required to comply with state and federal regulations to ensure a safe workplace for hospital personnel. The HPTs do not physically handle the $^{131}$I-MIBG vial or the patient but must perform roles in the patient’s room in the event of a spill and to ensure the regulatory compliance of the licensee. It is unlikely that external contamination confounded measurements of $^{131}$I in the thyroid. The radiation
exposures received by the Health Physics technicians monitored in this study are extremely low and well below regulatory limits.

**CONCLUSION**
Although health physics technicians receive an external exposure and a minimal uptake of $^{131}$I associated with performing tasks to monitor and decontaminate areas and personnel involved with $^{131}$I-MIBG therapy, measurement results obtained in this study demonstrate that exposure is well below NRC regulatory monitoring limits. Radiation exposure received by four health physics technicians during five separate $^{131}$I-MIBG therapy procedures were significantly low and present little, if any, risk to the technicians.
REFERENCES


# Appendix

Table 1 – Radiation exposure received by health physics technicians for each of the $^{131}$I-MIBG patient treatment procedures

<table>
<thead>
<tr>
<th>Treatment</th>
<th>$^{131}$I-MIBG Delivered (GBq)</th>
<th>External Dose Rate* (mR/hr)</th>
<th>HP Technician</th>
<th>Time in room (min)</th>
<th>Technician Dose (μSv)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15.6</td>
<td>50</td>
<td>A</td>
<td>73</td>
<td>6</td>
<td>1, 2</td>
</tr>
<tr>
<td>2</td>
<td>12.9</td>
<td>60</td>
<td>B</td>
<td>75</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>12.4</td>
<td>50</td>
<td>C</td>
<td>122</td>
<td>38</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>16.1</td>
<td>55</td>
<td>C</td>
<td>180</td>
<td>42</td>
<td>1</td>
</tr>
<tr>
<td>$5^A$</td>
<td>22.1</td>
<td>80</td>
<td>D</td>
<td>150</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>$5^B$</td>
<td>22.1</td>
<td>n/a</td>
<td>C</td>
<td>60</td>
<td>n/a</td>
<td>4</td>
</tr>
</tbody>
</table>

*: Initial dose rate measured at 1 m from patient.  
1: Infusion to room decontamination  
2: HPT has hypothyroid disease  
3: Infusion to patient release only  
4: Room decontamination only

Table 2 – Method 3 Thyroid Deposition Measurement

<table>
<thead>
<tr>
<th>Treatment</th>
<th>$^{131}$I-MIBG Delivered (GBq)</th>
<th>HPT</th>
<th>Work Time (min)</th>
<th>HPT Dose (μSv)</th>
<th>Thyroid Deposition (Bq)</th>
<th>Exposure to Whole Body Measurement</th>
<th>Decay Corrected Intake$^C$ (Bq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15.6</td>
<td>A</td>
<td>73</td>
<td>6</td>
<td>1.22 ± 0.40</td>
<td>~3hr</td>
<td>n/a$^D$</td>
</tr>
<tr>
<td>2</td>
<td>12.9</td>
<td>B</td>
<td>75</td>
<td>7</td>
<td>20.1 ± 1.30</td>
<td>~48hrs</td>
<td>134.9</td>
</tr>
<tr>
<td>3</td>
<td>12.4</td>
<td>C</td>
<td>122</td>
<td>38</td>
<td>3.95 ± 0.59</td>
<td>~48hrs</td>
<td>26.5</td>
</tr>
<tr>
<td>4</td>
<td>16.1</td>
<td>C</td>
<td>180</td>
<td>42</td>
<td>0.36 ± 0.22</td>
<td>~48hrs</td>
<td>2.4</td>
</tr>
<tr>
<td>$5^A$</td>
<td>22.1</td>
<td>D</td>
<td>150</td>
<td>17</td>
<td>0.08 ± 0.05</td>
<td>~48hrs</td>
<td>0.5</td>
</tr>
<tr>
<td>$5^B$</td>
<td>22.1</td>
<td>C</td>
<td>60</td>
<td>n/a</td>
<td>2.20 ± 0.40</td>
<td>~24hrs</td>
<td>16.5</td>
</tr>
</tbody>
</table>

A: Work completely prior to patient release  
B: Room decontamination post patient release  
C: Assumed source from unbound $^{131}$I  
D: HPT diagnosed with hypothyroidism
Figure 1 – RADOS RAD-60R Personal Pocket Electronic Dosimeter

Figure 2 - Canberra Osprey digital MCA with a collimated 2 inch x 2 inch NaI(Tl) detector
Figure 3 – Image of University of Cincinnati’s In Vivo Measurement Lab whole body counter

Figure 4 – Image of subject being counted in University of Cincinnati’s In Vivo Measurement Lab whole body counter
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